Fig. 1 A

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Wild          1 MATTAAAAAAALSAAATAKTGRKNHQRHHVLPARGRVGAAAVRCSAVSPVTPPSPAPPAT   60
P/R Mutant    1 MATTAAAAAAALSAAATAKTGRKNHQRHHVLPARGRVGAAAVRCSAVSPVTPPSPAPPAT   60
P/W Mutant    1 MATTAAAAAAALSAAATAKTGRKNHQRHHVLPARGRVGAAAVRCSAVSPVTPPSPAPPAT   60
P/S Mutant    1 MATTAAAAAAALSAAATAKTGRKNHQRHHVLPARGRVGAAAVRCSAVSPVTPPSPAPPAT   60
P/S/W Mutant  1 MATTAAAAAAALSAAATAKTGRKNHQRHHVLPARGRVGAAAVRCSAVSPVTPPSPAPPAT   60
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Wild         61 PLRPWGPAEPRKGADILVEALERCGVSDVFAYPGGASMEIHQALTRSPVITNHLFRHEQG   120
P/R Mutant   61 PLRPWGPAEPRKGADILVEALERCGVSDVFAYPGGASMEIHQALTRSPVITNHLFRHEQG   120
P/W Mutant   61 PLRPWGPAEPRKGADILVEALERCGVSDVFAYPGGASMEIHQALTRSPVITNHLFRHEQG   120
P/S Mutant   61 PLRPWGPAEPRKGADILVEALERCGVSDVFAYPGGASMEIHQALTRSPVITNHLFRHEQG   120
P/S/W Mutant 61 PLRPWGPAEPRKGADILVEALERCGVSDVFAYPGGASMEIHQALTRSPVITNHLFRHEQG   120
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Wild        121 EAFAASGYARASGRVGVCVATSGPGATNLVSALADALLDSVPMVAITGQVPRRMIGTDAF   180
P/R Mutant  121 EAFAASGYARASGRVGVCVATSGPGATNLVSALADALLDSVPMVAITGQVHSRMIGTDAF   180
P/W Mutant  121 EAFAASGYARASGRVGVCVATSGPGATNLVSALADALLDSVPMVAITGQVHRRMIGTDAF   180
P/S Mutant  121 EAFAASGYARASGRVGVCVATSGPGATNLVSALADALLDSVPMVAITGQVHRRMIGTDAF   180
P/S/W Mutant 121 EAFAASGYARASGRVGVCVATSGPGATNLVSALADALLDSVPMVAITGQVHRRMIGTDAF   180
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Wild        181 QETPIVEVTRSITKHNYLVLDVEDIPRVIQEAFFLASSGRPGPVLVDIPKDIQQQMAVPV   240
P/R Mutant  181 QETPIVEVTRSITKHNYLVLDVEDIPRVIQEAFFLASSGRPGPVLVDIPKDIQQQMAVPV   240
P/W Mutant  181 QETPIVEVTRSITKHNYLVLDVEDIPRVIQEAFFLASSGRPGPVLVDIPKDIQQQMAVPV   240
P/S Mutant  181 QETPIVEVTRSITKHNYLVLDVEDIPRVIQEAFFLASSGRPGPVLVDIPKDIQQQMAVPV   240
P/S/W Mutant 181 QETPIVEVTRSITKHNYLVLDVEDIPRVIQEAFFLASSGRPGPVLVDIPKDIQQQMAVPV   240
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Wild        241 WDTSMNLPGYIARLPKPPATELLEQVLRLVGESRRPILYVGGGCSASGDELRWFVELTGI   300
P/R Mutant  241 WDTSMNLPGYIARLPKPPATELLEQVLRLVGESRRPILYVGGGCSASGDELRWFVELTGI   300
P/W Mutant  241 WDTSMNLPGYIARLPKPPATELLEQVLRLVGESRRPILYVGGGCSASGDELRWFVELTGI   300
P/S Mutant  241 WDTSMNLPGYIARLPKPPATELLEQVLRLVGESRRPILYVGGGCSASGDELRWFVELTGI   300
P/S/W Mutant 241 WDTSMNLPGYIARLPKPPATELLEQVLRLVGESRRPILYVGGGCSASGDELRWFVELTGI   300
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Wild        301 PVTTTLMGLGNFPSDDPLSLRMLGMHGTVYANYAVDKADLLLAFGVRFDDRVTGKIEAFA   360
P/R Mutant  301 PVTTTLMGLGNFPSDDPLSLRMLGMHGTVYANYAVDKADLLLAFGVRFDDRVTGKIEAFA   360
P/W Mutant  301 PVTTTLMGLGNFPSDDPLSLRMLGMHGTVYANYAVDKADLLLAFGVRFDDRVTGKIEAFA   360
P/S Mutant  301 PVTTTLMGLGNFPSDDPLSLRMLGMHGTVYANYAVDKADLLLAFGVRFDDRVTGKIEAFA   360
P/S/W Mutant 301 PVTTTLMGLGNFPSDDPLSLRMLGMHGTVYANYAVDKADLLLAFGVRFDDRVTGKIEAFA   360
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Wild        361 SRAKIVHIDIDPAEIGKNKQPHVSICADVKLALQGLNALLQQSTTKTSSDFSAWHNELDQ   420
P/R Mutant  361 SRAKIVHIDIDPAEIGKNKQPHVSICADVKLALQGLNALLQQSTTKTSSDFSAWHNELDQ   420
P/W Mutant  361 SRAKIVHIDIDPAEIGKNKQPHVSICADVKLALQGLNALLQQSTTKTSSDFSAWHNELDQ   420
P/S Mutant  361 SRAKIVHIDIDPAEIGKNKQPHVSICADVKLALQGLNALLQQSTTKTSSDFSAWHNELDQ   420
P/S/W Mutant 361 SRAKIVHIDIDPAEIGKNKQPHVSICADVKLALQGLNALLQQSTTKTSSDFSAWHNELDQ   420
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Wild        421 QKREFPLGYKTFGEEIPPQYAIQVLDELTKGEAIIATGVGQHQMWAAQYYTYKRPRQWLS   480
P/R Mutant  421 QKREFPLGYKTFGEEIPPQYAIQVLDELTKGEAIIATGVGQHQMWAAQYYTYKRPRQWLS   480
P/W Mutant  421 QKREFPLGYKTFGEEIPPQYAIQVLDELTKGEAIIATGVGQHQMWAAQYYTYKRPRQWLS   480
P/S Mutant  421 QKREFPLGYKTFGEEIPPQYAIQVLDELTKGEAIIATGVGQHQMWAAQYYTYKRPRQWLS   480
P/S/W Mutant 421 QKREFPLGYKTFGEEIPPQYAIQVLDELTKGEAIIATGVGQHQMWAAQYYTYKRPRQWLS   480
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Wild        481 SAGLGAMGFGLPAAAGASVANPGVTVVDIDGDGSFLMNIQELALIRIENLPVKVMVLNNQ   540
P/R Mutant  481 SAGLGAMGFGLPAAAGASVANPGVTVVDIDGDGSFLMNIQELALIRIENLPVKVMVLNNQ   540
P/W Mutant  481 SAGLGAMGFGLPAAAGASVANPGVTVVDIDGDGSFLMNIQELALIRIENLPVKVMVLNNQ   540
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Fig. 1 B

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P/S Mutant      481 SAGLGAMGFGLPAAAGASVANPGVTVVDIDGDGSFLMNIQELALIRIENLPVKVMVLNNQ 540
P/S/W Mutant    481 SAGLGAMGFGLPAAAGASVANPGVTVVDIDGDGSFLMNIQELALIRIENLPVKVMVLNNQ 540
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Wild            541 HLGMVVQWEDRFYKANRAHTYLGNPECESEIYPDFVTIAKGFNIPAVRVTKKSEVRAAIK 600
P/R Mutant      541 HLGMVVQWEDRFYKANRAHTYLGNPECESEIYPDFVTIAKGFNIPAVRVTKKSEVRAAIK 600
P/W Mutant      541 HLGMVVQLEDRFYKANRAHTYLGNPECESEIYPDFVTIAKGFNIPAVRVTKKSEVRAAIK 600
P/S Mutant      541 HLGMVVQWEDRFYKANRAHTYLGNPECESEIYPDFVTIAKGFNIPAVRVTKKSEVRAAIK 600
P/S/W Mutant    541 HLGMVVQLEDRFYKANRAHTYLGNPECESEIYPDFVTIAKGFNIPAVRVTKKSEVRAAIK 600
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Wild            601 KMLETPGPYLLDIIVPHQEHVLPMIPSGGAFKDMILDGDGRTVY 644
P/R Mutant      601 KMLETPGPYLLDIIVPHQEHVLPMIPSGGAFKDMILDGDGRTVY 644
P/W Mutant      601 KMLETPGPYLLDIIVPHQEHVLPMIPSGGAFKDMILDGDGRTVY 644
P/S Mutant      601 KMLETPGPYLLDIIVPHQEHVLPMIPIGGAFKDMILDGDGRTVY 644
P/S/W Mutant    601 KMLETPGPYLLDIIVPHQEHVLPMIPIGGAFKDMILDGDGRTVY 644
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Fig. 2 A

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Wild              1 CCCAAACCCAGAAACCCTCGCCGCCGCCGCCGCCGCCGCCACCACCCACCATGGCTACGACCG   60
P/R Mutation      1 CCCAAACCCAGAAACCCTCGCCGCCGCCGCCGCCGCCGCCACCACCCACCATGGCTACGACCG   60
P/W Mutation      1 CCCAAACCCAGAAACCCTCGCCGCCGCCGCCGCCGCCGCCACCACCCACCATGGCTACGACCG   60
P/S Mutation      1 CCCAAACCCAGAAACCCTCGCCGCCGCCGCCGCCGCCGCCACCACCCACCATGGCTACGACCG   60
P/W/S Mutation    1 CCCAAACCCAGAAACCCTCGCCGCCGCCGCCGCCGCCGCCACCACCCACCATGGCTACGACCG   60
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Wild             61 CCGCGGCCGCGGCCGCCGCCCTGTCCGCCGCCGCGCGACGGCCAAGACCGGCCGTAAGAACC  120
P/R Mutation     61 CCGCGGCCGCGGCCGCCGCCCTGTCCGCCGCCGCGCGACGGCCAAGACCGGCCGTAAGAACC  120
P/W Mutation     61 CCGCGGCCGCGGCCGCCGCCCTGTCCGCCGCCGCGCGACGGCCAAGACCGGCCGTAAGAACC  120
P/S Mutation     61 CCGCGGCCGCGGCCGCCGCCCTGTCCGCCGCCGCGCGACGGCCAAGACCGGCCGTAAGAACC  120
P/W/S Mutation   61 CCGCGGCCGCGGCCGCCGCCCTGTCCGCCGCCGCGCGACGGCCAAGACCGGCCGTAAGAACC  120
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Wild            121 ACCAGCGACACCACGTCCTTCCCGCTCGAGGCCGGGTGGGGGCGGCGGCGGTCAGGTGCT  180
P/R Mutation    121 ACCAGCGACACCACGTCCTTCCCGCTCGAGGCCGGGTGGGGGCGGCGGCGGTCAGGTGCT  180
P/W Mutation    121 ACCAGCGACACCACGTCCTTCCCGCTCGAGGCCGGGTGGGGGCGGCGGCGGTCAGGTGCT  180
P/S Mutation    121 ACCAGCGACACCACGTCCTTCCCGCTCGAGGCCGGGTGGGGGCGGCGGCGGTCAGGTGCT  180
P/W/S Mutation  121 ACCAGCGACACCACGTCCTTCCCGCTCGAGGCCGGGTGGGGGCGGCGGCGGTCAGGTGCT  180
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Wild            181 CGGCGGTGTCCCCGGTCACCCCGCCGTCCCCGGCGCCGCCGGCCACGCCGCTCCGGCCGT  240
P/R Mutation    181 CGGCGGTGTCCCCGGTCACCCCGCCGTCCCCGGCGCCGCCGGCCACGCCGCTCCGGCCGT  240
P/W Mutation    181 CGGCGGTGTCCCCGGTCACCCCGCCGTCCCCGGCGCCGCCGGCCACGCCGCTCCGGCCGT  240
P/S Mutation    181 CGGCGGTGTCCCCGGTCACCCCGCCGTCCCCGGCGCCGCCGGCCACGCCGCTCCGGCCGT  240
P/W/S Mutation  181 CGGCGGTGTCCCCGGTCACCCCGCCGTCCCCGGCGCCGCCGGCCACGCCGCTCCGGCCGT  240
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Wild            241 GGGGGCCGGCCGAGCCCCGCAAGGGCGCGGACATCCTCGTGGAGGCGCTGGAGCGGTGCG  300
P/R Mutation    241 GGGGGCCGGCCGAGCCCCGCAAGGGCGCGGACATCCTCGTGGAGGCGCTGGAGCGGTGCG  300
P/W Mutation    241 GGGGGCCGGCCGAGCCCCGCAAGGGCGCGGACATCCTCGTGGAGGCGCTGGAGCGGTGCG  300
P/S Mutation    241 GGGGGCCGGCCGAGCCCCGCAAGGGCGCGGACATCCTCGTGGAGGCGCTGGAGCGGTGCG  300
P/W/S Mutation  241 GGGGGCCGGCCGAGCCCCGCAAGGGCGCGGACATCCTCGTGGAGGCGCTGGAGCGGTGCG  300
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Wild            301 GCGTCAGCGACGTGTTCGCCTACCCGGGCGGCGCGTCCATGGAGATCCACCAGGCGCTGA  360
P/R Mutation    301 GCGTCAGCGACGTGTTCGCCTACCCGGGCGGCGCGTCCATGGAGATCCACCAGGCGCTGA  360
P/W Mutation    301 GCGTCAGCGACGTGTTCGCCTACCCGGGCGGCGCGTCCATGGAGATCCACCAGGCGCTGA  360
P/S Mutation    301 GCGTCAGCGACGTGTTCGCCTACCCGGGCGGCGCGTCCATGGAGATCCACCAGGCGCTGA  360
P/W/S Mutation  301 GCGTCAGCGACGTGTTCGCCTACCCGGGCGGCGCGTCCATGGAGATCCACCAGGCGCTGA  360
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Wild            361 CGCGCTCCCCGGTCATCACCAACCACCTCTTCCGCCACGAGCAGGGCGAGGCGTTCGCGG  420
P/R Mutation    361 CGCGCTCCCCGGTCATCACCAACCACCTCTTCCGCCACGAGCAGGGCGAGGCGTTCGCGG  420
P/W Mutation    361 CGCGCTCCCCGGTCATCACCAACCACCTCTTCCGCCACGAGCAGGGCGAGGCGTTCGCGG  420
P/S Mutation    361 CGCGCTCCCCGGTCATCACCAACCACCTCTTCCGCCACGAGCAGGGCGAGGCGTTCGCGG  420
P/W/S Mutation  361 CGCGCTCCCCGGTCATCACCAACCACCTCTTCCGCCACGAGCAGGGCGAGGCGTTCGCGG  420
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Wild            421 CGTCCGGGTACGCGCGCGCGTCCGGCCGCGTCGGGGTCTGCGTCGCCACCTCCGGCCCCG  480
P/R Mutation    421 CGTCCGGGTACGCGCGCGCGTCCGGCCGCGTCGGGGTCTGCGTCGCCACCTCCGGCCCCG  480
P/W Mutation    421 CGTCCGGGTACGCGCGCGCGTCCGGCCGCGTCGGGGTCTGCGTCGCCACCTCCGGCCCCG  480
P/S Mutation    421 CGTCCGGGTACGCGCGCGCGTCCGGCCGCGTCGGGGTCTGCGTCGCCACCTCCGGCCCCG  480
P/W/S Mutation  421 CGTCCGGGTACGCGCGCGCGTCCGGCCGCGTCGGGGTCTGCGTCGCCACCTCCGGCCCCG  480
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Wild            481 GGGCAACCAACCTCGTGTCCGCGCTCGCCGACGCGCTGCTCGACTCCGTCCCGATGGTCG  540
P/R Mutation    481 GGGCAACCAACCTCGTGTCCGCGCTCGCCGACGCGCTGCTCGACTCCGTCCCGATGGTCG  540
P/W Mutation    481 GGGCAACCAACCTCGTGTCCGCGCTCGCCGACGCGCTGCTCGACTCCGTCCCGATGGTCG  540
P/S Mutation    481 GGGCAACCAACCTCGTGTCCGCGCTCGCCGACGCGCTGCTCGACTCCGTCCCGATGGTCG  540
P/W/S Mutation  481 GGGCAACCAACCTCGTGTCCGCGCTCGCCGACGCGCTGCTCGACTCCGTCCCGATGGTCG  540
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Wild            541 CCATCACGGGCCAGGTCCCCCGCCGCATGATCGGCACCGACGCCTTCCAGGAGACGCCCA  600
P/R Mutation    541 CCATCACGGGCCAGGTCCACAGCCGCATGATCGGCACCGACGCCTTCCAGGAGACGCCCA  600
P/W Mutation    541 CCATCACGGGCCAGGTCCACCGCCGCATGATCGGCACCGACGCCTTCCAGGAGACGCCCA  600
P/S Mutation    541 CCATCACGGGCCAGGTCCACCGCCGCATGATCGGCACCGACGCCTTCCAGGAGACGCCCA  600
P/W/S Mutation  541 CCATCACGGGCCAGGTCCACCGCCGCATGATCGGCACCGACGCCTTCCAGGAGACGCCCA  600
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Wild            601 TAGTCGAGGTCACCCGCTCCATCACCAAGCACAATTACCTTGTCCTTGATGTGGAGGACA  660
P/R Mutation    601 TAGTCGAGGTCACCCGCTCCATCACCAAGCACAATTACCTTGTCCTTGATGTGGAGGACA  660
P/W Mutation    601 TAGTCGAGGTCACCCGCTCCATCACCAAGCACAATTACCTTGTCCTTGATGTGGAGGACA  660
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Fig. 2 B

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P/S Mutation      601 TAGTCGAGGTCACCCGCTCCATCACCAAGCACAATTACCTTGTCCTTGATGTGGAGGACA  660
P/W/S Mutation    601 TAGTCGAGGTCACCCGCTCCATCACCAAGCACAATTACCTTGTCCTTGATGTGGAGGACA  660
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Wild              661 TCCCCCGCGTCATACAGGAAGCCTTCTTCCTCGCGTCCTCGGGCCGTCCTGGCCCGGTGC  720
P/R Mutation      661 TCCCCCGCGTCATACAGGAAGCCTTCTTCCTCGCGTCCTCGGGCCGTCCTGGCCCGGTGC  720
P/W Mutation      661 TCCCCCGCGTCATACAGGAAGCCTTCTTCCTCGCGTCCTCGGGCCGTCCTGGCCCGGTGC  720
P/S Mutation      661 TCCCCCGCGTCATACAGGAAGCCTTCTTCCTCGCGTCCTCGGGCCGTCCTGGCCCGGTGC  720
P/W/S Mutation    661 TCCCCCGCGTCATACAGGAAGCCTTCTTCCTCGCGTCCTCGGGCCGTCCTGGCCCGGTGC  720
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Wild              721 TGGTCGACATCCCCAAGGACATCCAGCAGCAGATGGCCGTGCCGGTCTGGGACACCTCGA  780
P/R Mutation      721 TGGTCGACATCCCCAAGGACATCCAGCAGCAGATGGCCGTGCCGGTCTGGGACACCTCGA  780
P/W Mutation      721 TGGTCGACATCCCCAAGGACATCCAGCAGCAGATGGCCGTGCCGGTCTGGGACACCTCGA  780
P/S Mutation      721 TGGTCGACATCCCCAAGGACATCCAGCAGCAGATGGCCGTGCCGGTCTGGGACACCTCGA  780
P/W/S Mutation    721 TGGTCGACATCCCCAAGGACATCCAGCAGCAGATGGCCGTGCCGGTCTGGGACACCTCGA  780
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Wild              781 TGAATCTACCAGGGTACATCGCACGCCTGCCCAAGCCACCCGCGACAGAATTGCTTGAGC  840
P/R Mutation      781 TGAATCTACCAGGGTACATCGCACGCCTGCCCAAGCCACCCGCGACAGAATTGCTTGAGC  840
P/W Mutation      781 TGAATCTACCAGGGTACATCGCACGCCTGCCCAAGCCACCCGCGACAGAATTGCTTGAGC  840
P/S Mutation      781 TGAATCTACCAGGGTACATCGCACGCCTGCCCAAGCCACCCGCGACAGAATTGCTTGAGC  840
P/W/S Mutation    781 TGAATCTACCAGGGTACATCGCACGCCTGCCCAAGCCACCCGCGACAGAATTGCTTGAGC  840
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Wild              841 AGGTCTTGCGTCTGGTTGGCGAGTCACGGCGCCCGATTCTCTATGTCGGTGGTGGCTGCT  900
P/R Mutation      841 AGGTCTTGCGTCTGGTTGGCGAGTCACGGCGCCCGATTCTCTATGTCGGTGGTGGCTGCT  900
P/W Mutation      841 AGGTCTTGCGTCTGGTTGGCGAGTCACGGCGCCCGATTCTCTATGTCGGTGGTGGCTGCT  900
P/S Mutation      841 AGGTCTTGCGTCTGGTTGGCGAGTCACGGCGCCCGATTCTCTATGTCGGTGGTGGCTGCT  900
P/W/S Mutation    841 AGGTCTTGCGTCTGGTTGGCGAGTCACGGCGCCCGATTCTCTATGTCGGTGGTGGCTGCT  900
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Wild              901 CTGCATCTGGTGACGAATTGCGCTGGTTTGTTGAGCTGACTGGTATCCCAGTTACAACCA  960
P/R Mutation      901 CTGCATCTGGTGACGAATTGCGCTGGTTTGTTGAGCTGACTGGTATCCCAGTTACAACCA  960
P/W Mutation      901 CTGCATCTGGTGACGAATTGCGCTGGTTTGTTGAGCTGACTGGTATCCCAGTTACAACCA  960
P/S Mutation      901 CTGCATCTGGTGACGAATTGCGCTGGTTTGTTGAGCTGACTGGTATCCCAGTTACAACCA  960
P/W/S Mutation    901 CTGCATCTGGTGACGAATTGCGCTGGTTTGTTGAGCTGACTGGTATCCCAGTTACAACCA  960
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Wild              961 CTCTGATGGGCCTCGGCAATTTCCCCAGTGACGACCCGTTGTCCCTGCGCATGCTTGGGA 1020
P/R Mutation      961 CTCTGATGGGCCTCGGCAATTTCCCCAGTGACGACCCGTTGTCCCTGCGCATGCTTGGGA 1020
P/W Mutation      961 CTCTGATGGGCCTCGGCAATTTCCCCAGTGACGACCCGTTGTCCCTGCGCATGCTTGGGA 1020
P/S Mutation      961 CTCTGATGGGCCTCGGCAATTTCCCCAGTGACGACCCGTTGTCCCTGCGCATGCTTGGGA 1020
P/W/S Mutation    961 CTCTGATGGGCCTCGGCAATTTCCCCAGTGACGACCCGTTGTCCCTGCGCATGCTTGGGA 1020
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Wild             1021 TGCATGGCACGGTGTACGCAAATTATGCCGTGGATAAGGCTGACCTGTTGCTTGCGTTTG 1080
P/R Mutation     1021 TGCATGGCACGGTGTACGCAAATTATGCCGTGGATAAGGCTGACCTGTTGCTTGCGTTTG 1080
P/W Mutation     1021 TGCATGGCACGGTGTACGCAAATTATGCCGTGGATAAGGCTGACCTGTTGCTTGCGTTTG 1080
P/S Mutation     1021 TGCATGGCACGGTGTACGCAAATTATGCCGTGGATAAGGCTGACCTGTTGCTTGCGTTTG 1080
P/W/S Mutation   1021 TGCATGGCACGGTGTACGCAAATTATGCCGTGGATAAGGCTGACCTGTTGCTTGCGTTTG 1080
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Wild             1081 GTGTGCGGTTTGATGATCGTGTGACAGGGAAAATTGAGGCTTTTGCAAGCAGGGCCAAGA 1140
P/R Mutation     1081 GTGTGCGGTTTGATGATCGTGTGACAGGGAAAATTGAGGCTTTTGCAAGCAGGGCCAAGA 1140
P/W Mutation     1081 GTGTGCGGTTTGATGATCGTGTGACAGGGAAAATTGAGGCTTTTGCAAGCAGGGCCAAGA 1140
P/S Mutation     1081 GTGTGCGGTTTGATGATCGTGTGACAGGGAAAATTGAGGCTTTTGCAAGCAGGGCCAAGA 1140
P/W/S Mutation   1081 GTGTGCGGTTTGATGATCGTGTGACAGGGAAAATTGAGGCTTTTGCAAGCAGGGCCAAGA 1140
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Wild             1141 TTGTGCACATTGACATTGATCCAGCAGAGATTGGAAAGAACAAGCAACCACATGTGTCAA 1200
P/R Mutation     1141 TTGTGCACATTGACATTGATCCAGCAGAGATTGGAAAGAACAAGCAACCACATGTGTCAA 1200
P/W Mutation     1141 TTGTGCACATTGACATTGATCCAGCAGAGATTGGAAAGAACAAGCAACCACATGTGTCAA 1200
P/S Mutation     1141 TTGTGCACATTGACATTGATCCAGCAGAGATTGGAAAGAACAAGCAACCACATGTGTCAA 1200
P/W/S Mutation   1141 TTGTGCACATTGACATTGATCCAGCAGAGATTGGAAAGAACAAGCAACCACATGTGTCAA 1200
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Wild             1201 TTTGCGCAGATGTTAAGCTTGCTTTACAGGGCTTGAATGCTCTGCTACAACAGAGCACAA 1260
P/R Mutation     1201 TTTGCGCAGATGTTAAGCTTGCTTTACAGGGCTTGAATGCTCTGCTACAACAGAGCACAA 1260
P/W Mutation     1201 TTTGCGCAGATGTTAAGCTTGCTTTACAGGGCTTGAATGCTCTGCTACAACAGAGCACAA 1260
P/S Mutation     1201 TTTGCGCAGATGTTAAGCTTGCTTTACAGGGCTTGAATGCTCTGCTACAACAGAGCACAA 1260
P/W/S Mutation   1201 TTTGCGCAGATGTTAAGCTTGCTTTACAGGGCTTGAATGCTCTGCTACAACAGAGCACAA 1260
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Wild             1261 CAAAGACAAGTTCTGATTTTAGTGCATGGCACAATGAGTTGGACCAGCAGAAGAGGGAGT 1320
P/R Mutation     1261 CAAAGACAAGTTCTGATTTTAGTGCATGGCACAATGAGTTGGACCAGCAGAAGAGGGAGT 1320
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Fig. 2 C

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P/W Mutation    1261 CAAAGACAAGTTCTGATTTTAGTGCATGGCACAATGAGTTGGACCAGCAGAAGAGGGAGT 1320
P/S Mutation    1261 CAAAGACAAGTTCTGATTTTAGTGCATGGCACAATGAGTTGGACCAGCAGAAGAGGGAGT 1320
P/W/S Mutation  1261 CAAAGACAAGTTCTGATTTTAGTGCATGGCACAATGAGTTGGACCAGCAGAAGAGGGAGT 1320
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Wild            1321 TTCCTCTGGGGTACAAAACTTTTGGTGAAGAGATCCCACCGCAATATGCCATTCAGGTGC 1380
P/R Mutation    1321 TTCCTCTGGGGTACAAAACTTTTGGTGAAGAGATCCCACCGCAATATGCCATTCAGGTGC 1380
P/W Mutation    1321 TTCCTCTGGGGTACAAAACTTTTGGTGAAGAGATCCCACCGCAATATGCCATTCAGGTGC 1380
P/S Mutation    1321 TTCCTCTGGGGTACAAAACTTTTGGTGAAGAGATCCCACCGCAATATGCCATTCAGGTGC 1380
P/W/S Mutation  1321 TTCCTCTGGGGTACAAAACTTTTGGTGAAGAGATCCCACCGCAATATGCCATTCAGGTGC 1380
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Wild            1381 TGGATGAGCTGACGAAAGGTGAGGCAATCATCGCTACTGGTGTTGGGCAGCACCAGATGT 1440
P/R Mutation    1381 TGGATGAGCTGACGAAAGGTGAGGCAATCATCGCTACTGGTGTTGGGCAGCACCAGATGT 1440
P/W Mutation    1381 TGGATGAGCTGACGAAAGGTGAGGCAATCATCGCTACTGGTGTTGGGCAGCACCAGATGT 1440
P/S Mutation    1381 TGGATGAGCTGACGAAAGGTGAGGCAATCATCGCTACTGGTGTTGGGCAGCACCAGATGT 1440
P/W/S Mutation  1381 TGGATGAGCTGACGAAAGGTGAGGCAATCATCGCTACTGGTGTTGGGCAGCACCAGATGT 1440
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Wild            1441 GGGCGGCACAATATTACACCTACAAGCGGCCACGGCAGTGGCTGTCTTCGGCTGGTCTGG 1500
P/R Mutation    1441 GGGCGGCACAATATTACACCTACAAGCGGCCACGGCAGTGGCTGTCTTCGGCTGGTCTGG 1500
P/W Mutation    1441 GGGCGGCACAATATTACACCTACAAGCGGCCACGGCAGTGGCTGTCTTCGGCTGGTCTGG 1500
P/S Mutation    1441 GGGCGGCACAATATTACACCTACAAGCGGCCACGGCAGTGGCTGTCTTCGGCTGGTCTGG 1500
P/W/S Mutation  1441 GGGCGGCACAATATTACACCTACAAGCGGCCACGGCAGTGGCTGTCTTCGGCTGGTCTGG 1500
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Wild            1501 GCGCAATGGGATTTGGGCTGCCTGCTGCAGCTGGTGCTTCTGTGGCTAACCCAGGTGTCA 1560
P/R Mutation    1501 GCGCAATGGGATTTGGGCTGCCTGCTGCAGCTGGTGCTTCTGTGGCTAACCCAGGTGTCA 1560
P/W Mutation    1501 GCGCAATGGGATTTGGGCTGCCTGCTGCAGCTGGTGCTTCTGTGGCTAACCCAGGTGTCA 1560
P/S Mutation    1501 GCGCAATGGGATTTGGGCTGCCTGCTGCAGCTGGTGCTTCTGTGGCTAACCCAGGTGTCA 1560
P/W/S Mutation  1501 GCGCAATGGGATTTGGGCTGCCTGCTGCAGCTGGTGCTTCTGTGGCTAACCCAGGTGTCA 1560
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Wild            1561 CAGTTGTTGATATTGATGGGGATGGTAGCTTCCTCATGAACATTCAGGAGCTGGCATTGA 1620
P/R Mutation    1561 CAGTTGTTGATATTGATGGGGATGGTAGCTTCCTCATGAACATTCAGGAGCTGGCATTGA 1620
P/W Mutation    1561 CAGTTGTTGATATTGATGGGGATGGTAGCTTCCTCATGAACATTCAGGAGCTGGCATTGA 1620
P/S Mutation    1561 CAGTTGTTGATATTGATGGGGATGGTAGCTTCCTCATGAACATTCAGGAGCTGGCATTGA 1620
P/W/S Mutation  1561 CAGTTGTTGATATTGATGGGGATGGTAGCTTCCTCATGAACATTCAGGAGCTGGCATTGA 1620
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Wild            1621 TCCGCATTGAGAACCTCCCTGTGAAGGTGATGGTGTTGAACAACCAACATTTGGGTATGG 1680
P/R Mutation    1621 TCCGCATTGAGAACCTCCCTGTGAAGGTGATGGTGTTGAACAACCAACATTTGGGTATGG 1680
P/W Mutation    1621 TCCGCATTGAGAACCTCCCTGTGAAGGTGATGGTGTTGAACAACCAACATTTGGGTATGG 1680
P/S Mutation    1621 TCCGCATTGAGAACCTCCCTGTGAAGGTGATGGTGTTGAACAACCAACATTTGGGTATGG 1680
P/W/S Mutation  1621 TCCGCATTGAGAACCTCCCTGTGAAGGTGATGGTGTTGAACAACCAACATTTGGGTATGG 1680
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Wild            1681 TGGTGCAATGGGAGGATAGGTTTTACAAGGCGAATAGGGCGCATACATACTTGGGCAACC 1740
P/R Mutation    1681 TGGTGCAATGGGAGGATAGGTTTTACAAGGCGAATAGGGCGCATACATACTTGGGCAACC 1740
P/W Mutation    1681 TGGTGCAATTGGAGGATAGGTTTTACAAGGCGAATAGGGCGCATACATACTTGGGCAACC 1740
P/S Mutation    1681 TGGTGCAATGGGAGGATAGGTTTTACAAGGCGAATAGGGCGCATACATACTTGGGCAACC 1740
P/W/S Mutation  1681 TGGTGCAATTGGAGGATAGGTTTTACAAGGCGAATAGGGCGCATACATACTTGGGCAACC 1740
                     *********.**************************************************

Wild            1741 CGGAATGTGAGAGCGAGATATATCCAGATTTTGTGACTATTGCTAAGGGGTTCAATATTC 1800
P/R Mutation    1741 CGGAATGTGAGAGCGAGATATATCCAGATTTTGTGACTATTGCTAAGGGGTTCAATATTC 1800
P/W Mutation    1741 CGGAATGTGAGAGCGAGATATATCCAGATTTTGTGACTATTGCTAAGGGGTTCAATATTC 1800
P/S Mutation    1741 CGGAATGTGAGAGCGAGATATATCCAGATTTTGTGACTATTGCTAAGGGGTTCAATATTC 1800
P/W/S Mutation  1741 CGGAATGTGAGAGCGAGATATATCCAGATTTTGTGACTATTGCTAAGGGGTTCAATATTC 1800
                     ************************************************************

Wild            1801 CTGCAGTCCGTGTAACAAAGAAGAGTGAAGTCCGTGCCGCCATCAAGAAGATGCTCGAGA 1860
P/R Mutation    1801 CTGCAGTCCGTGTAACAAAGAAGAGTGAAGTCCGTGCCGCCATCAAGAAGATGCTCGAGA 1860
P/W Mutation    1801 CTGCAGTCCGTGTAACAAAGAAGAGTGAAGTCCGTGCCGCCATCAAGAAGATGCTCGAGA 1860
P/S Mutation    1801 CTGCAGTCCGTGTAACAAAGAAGAGTGAAGTCCGTGCCGCCATCAAGAAGATGCTCGAGA 1860
P/W/S Mutation  1801 CTGCAGTCCGTGTAACAAAGAAGAGTGAAGTCCGTGCCGCCATCAAGAAGATGCTCGAGA 1860
                     ************************************************************

Wild            1861 CTCCAGGGCCATACTTGTTGGATATCATCGTCCCGCACCAGGAGCATGTGCTGCCTATGA 1920
P/R Mutation    1861 CTCCAGGGCCATACTTGTTGGATATCATCGTCCCGCACCAGGAGCATGTGCTGCCTATGA 1920
P/W Mutation    1861 CTCCAGGGCCATACTTGTTGGATATCATCGTCCCGCACCAGGAGCATGTGCTGCCTATGA 1920
P/S Mutation    1861 CTCCAGGGCCATACTTGTTGGATATCATCGTCCCGCACCAGGAGCATGTGCTGCCTATGA 1920
P/W/S Mutation  1861 CTCCAGGGCCATACTTGTTGGATATCATCGTCCCGCACCAGGAGCATGTGCTGCCTATGA 1920
                     ************************************************************

Wild            1921 TCCCAAGTGGGGGCGCATTCAAGGACATGATCCTGGATGGTGATGGCAGGACTGTGTATT 1980
```

Fig. 2 D

```
P/R Mutation     1921 TCCCAAGTGGGGGCGCATTCAAGGACATGATCCTGGATGGTGATGGCAGGACTGTGTATT 1980
P/W Mutation     1921 TCCCAAGTGGGGGCGCATTCAAGGACATGATCCTGGATGGTGATGGCAGGACTGTGTATT 1980
P/S Mutation     1921 TCCCAATTGGGGGCGCATTCAAGGACATGATCCTGGATGGTGATGGCAGGACTGTGTATT 1980
P/W/S Mutation   1921 TCCCAATTGGGGGCGCATTCAAGGACATGATCCTGGATGGTGATGGCAGGACTGTGTATT 1980
                      *******.**************************************************

Wild             1981 AATCTATAATCTGTATGTTGGCAAAGCACCAGCCCGGCCTATGTTTGACCTGAATGACCC 2040
P/R Mutation     1981 AATCTATAATCTGTATGTTGGCAAAGCACCAGCCCGGCCTATGTTTGACCTGAATGACCC 2040
P/W Mutation     1981 AATCTATAATCTGTATGTTGGCAAAGCACCAGCCCGGCCTATGTTTGACCTGAATGACCC 2040
P/S Mutation     1981 AATCTATAATCTGTATGTTGGCAAAGCACCAGCCCGGCCTATGTTTGACCTGAATGACCC 2040
P/W/S Mutation   1981 AATCTATAATCTGTATGTTGGCAAAGCACCAGCCCGGCCTATGTTTGACCTGAATGACCC 2040
                      ************************************************************

Wild             2041 ATAAAGAGTGGTATGCCTATGATGTTTGTATGTGCTCTATCAATAACTAAGGTGTCAACT 2100
P/R Mutation     2041 ATAAAGAGTGGTATGCCTATGATGTTTGTATGTGCTCTATCAATAACTAAGGTGTCAACT 2100
P/W Mutation     2041 ATAAAGAGTGGTATGCCTATGATGTTTGTATGTGCTCTATCAATAACTAAGGTGTCAACT 2100
P/S Mutation     2041 ATAAAGAGTGGTATGCCTATGATGTTTGTATGTGCTCTATCAATAACTAAGGTGTCAACT 2100
P/W/S Mutation   2041 ATAAAGAGTGGTATGCCTATGATGTTTGTATGTGCTCTATCAATAACTAAGGTGTCAACT 2100
                      ************************************************************

Wild             2101 ATGAACCATATGCTCTTCTGTTTTACTTGTTTGATGTGCTTGGCATGGTAATCCTAATTA 2160
P/R Mutation     2101 ATGAACCATATGCTCTTCTGTTTTACTTGTTTGATGTGCTTGGCATGGTAATCCTAATTA 2160
P/W Mutation     2101 ATGAACCATATGCTCTTCTGTTTTACTTGTTTGATGTGCTTGGCATGGTAATCCTAATTA 2160
P/S Mutation     2101 ATGAACCATATGCTCTTCTGTTTTACTTGTTTGATGTGCTTGGCATGGTAATCCTAATTA 2160
P/W/S Mutation   2101 ATGAACCATATGCTCTTCTGTTTTACTTGTTTGATGTGCTTGGCATGGTAATCCTAATTA 2160
                      ************************************************************

Wild             2161 GCTTCCTGCTGTCTAGGTTTGTAGTGTGTTGTTTTCTGTAGGCATATGCATCACAAGATA 2220
P/R Mutation     2161 GCTTCCTGCTGTCTAGGTTTGTAGTGTGTTGTTTTCTGTAGGCATATGCATCACAAGATA 2220
P/W Mutation     2161 GCTTCCTGCTGTCTAGGTTTGTAGTGTGTTGTTTTCTGTAGGCATATGCATCACAAGATA 2220
P/S Mutation     2161 GCTTCCTGCTGTCTAGGTTTGTAGTGTGTTGTTTTCTGTAGGCATATGCATCACAAGATA 2220
P/W/S Mutation   2161 GCTTCCTGCTGTCTAGGTTTGTAGTGTGTTGTTTTCTGTAGGCATATGCATCACAAGATA 2220
                      ************************************************************

Wild             2221 TCATGTAAGTTTCTTGTCCTACATATCAATAATAAGAGAATAAAGTACTTCTATGCAAAA 2280
P/R Mutation     2221 TCATGTAAGTTTCTTGTCCTACATATCAATAATAAGAGAATAAAGTACTTCTATGCAAAA 2280
P/W Mutation     2221 TCATGTAAGTTTCTTGTCCTACATATCAATAATAAGAGAATAAAGTACTTCTATGCAAAA 2280
P/S Mutation     2221 TCATGTAAGTTTCTTGTCCTACATATCAATAATAAGAGAATAAAGTACTTCTATGTAAAA 2280
P/W/S Mutation   2221 TCATGTAAGTTTCTTGTCCTACATATCAATAATAAGAGAATAAAGTACTTCTATGTAAAA 2280
                      ************************************************.*****

Wild             2281 AAAAAAAAAAAAAAAAAAAAA                                    2301
P/R Mutation     2281 AAAAAAAAAAAAAAAAAAAAA                                    2301
P/W Mutation     2281 AAAAAAAAAAAAAAAAAAAA                                    2300
P/S Mutation     2281 AAAAAAAAAAAAAA                                          2294
P/W/S Mutation   2281 AAAAAAAAAAAAAA                                          2294
                      **************......
```

Fig.3

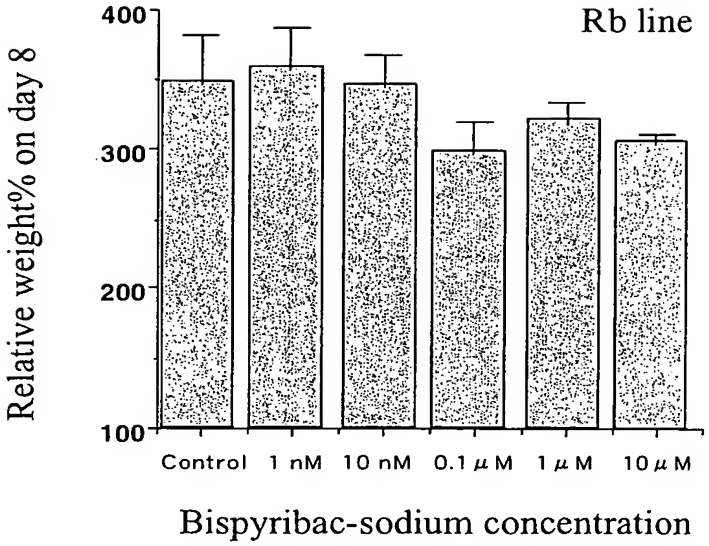
Rb line
Relative weight% on day 8
400
300
200
100
Control
1 nM
10 nM
0.1 μM
1 μM
10 μM
Bispyribac-sodium concentration

Fig. 4

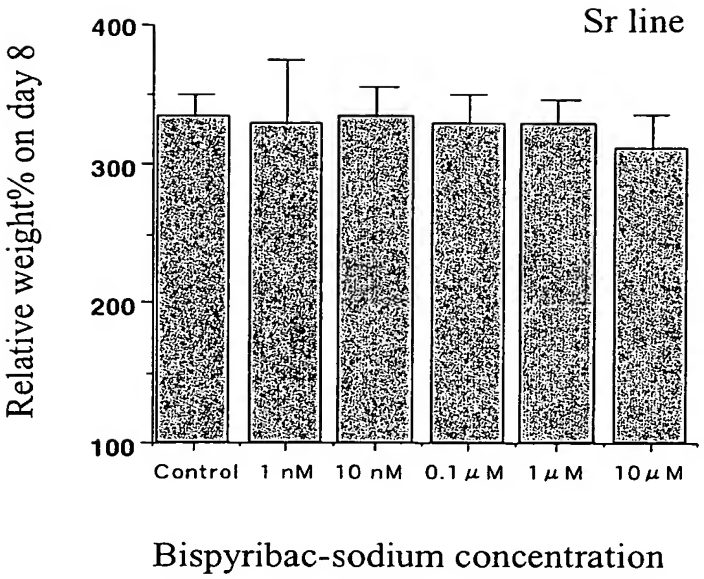
Sr line
Relative weight% on day 8
400
300
200
100
Control
1 nM
10 nM
0.1 μM
1 μM
10 μM
Bispyribac-sodium concentration

Fig. 5

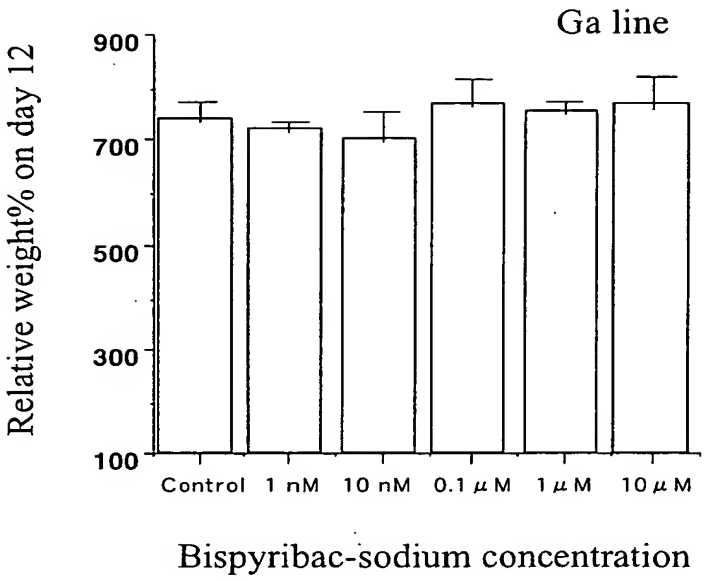
Ga line
Relative weight% on day 12
900
700
500
300
100
Control
1 nM
10 nM
0.1 μM
1 μM
10 μM
Bispyribac-sodium concentration

Fig. 6

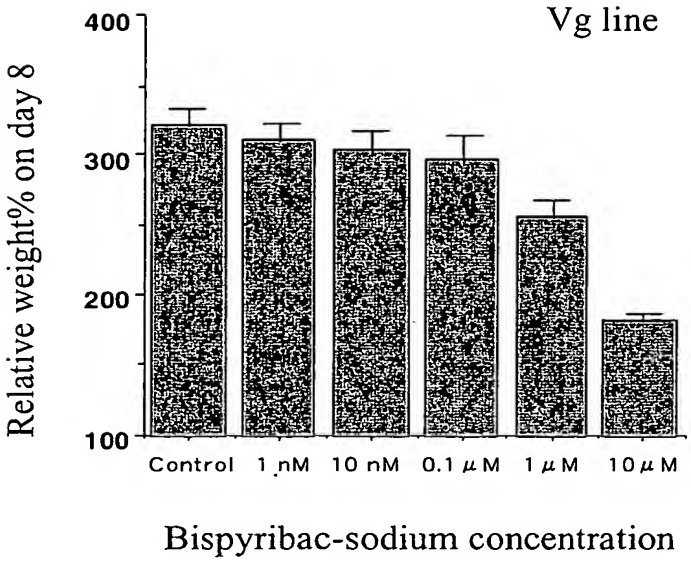
Vg line
Relative weight% on day 8
400
300
200
100
Control
1 nM
10 nM
0.1 μM
1 μM
10 μM
Bispyribac-sodium concentration

Fig. 7

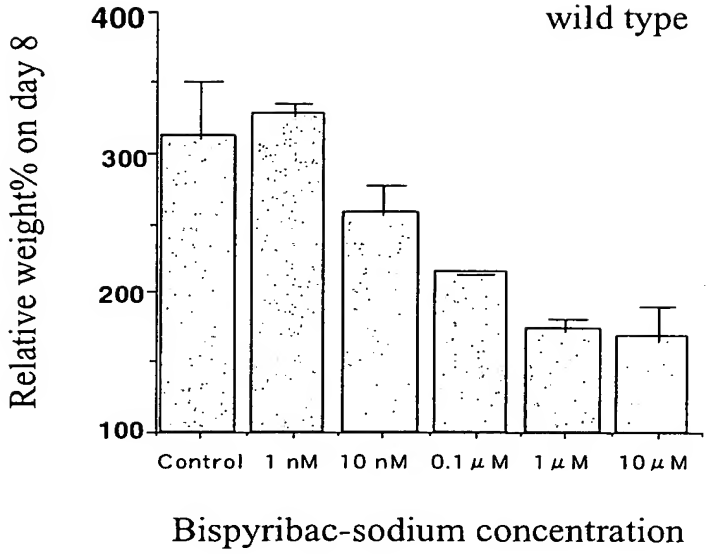
wild type
400
300
200
100
Relative weight% on day 8
Control
1 nM
10 nM
0.1 μM
1 μM
10 μM
Bispyribac-sodium concentration

Fig. 8

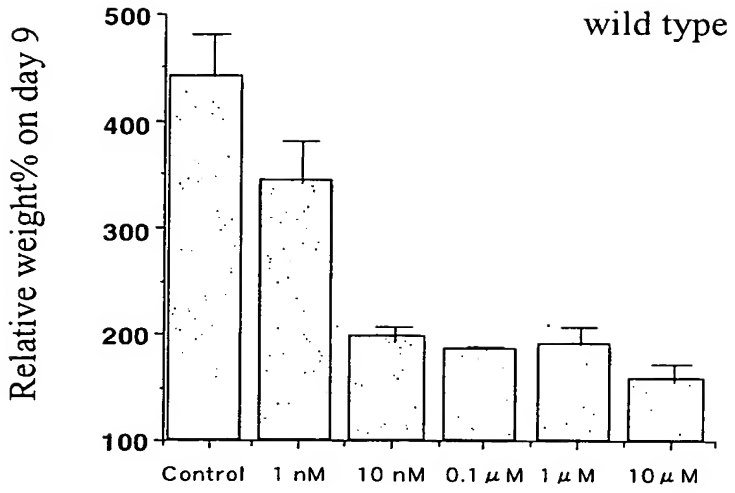
wild type
Relative weight% on day 9
500
400
300
200
100
Control
1 nM
10 nM
0.1 μM
1 μM
10 μM
Chlorsulfuron concentration

Fig. 9

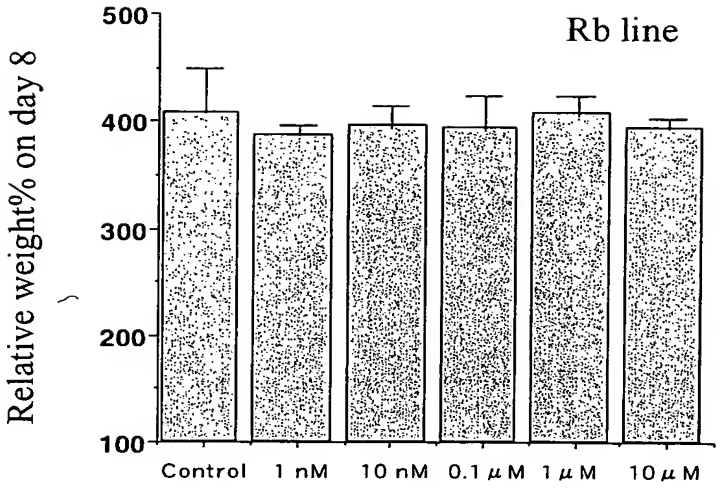
Rb line
Relative weight% on day 8
500
400
300
200
100
Control
1 nM
10 nM
0.1 μM
1 μM
10 μM
Chlorsulfuron concentration

Fig. 1 0

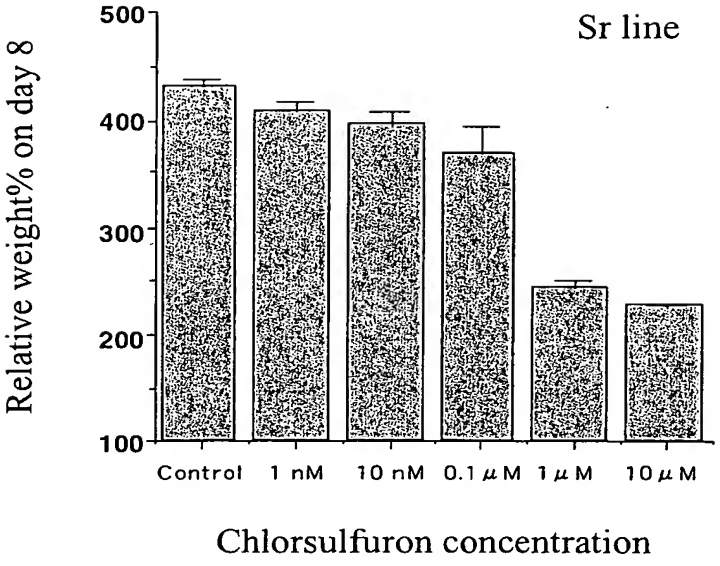
Sr line
Relative weight% on day 8
500
400
300
200
100
Control
1 nM
10 nM
0.1 μM
1 μM
10 μM
Chlorsulfuron concentration

Fig. 1 1

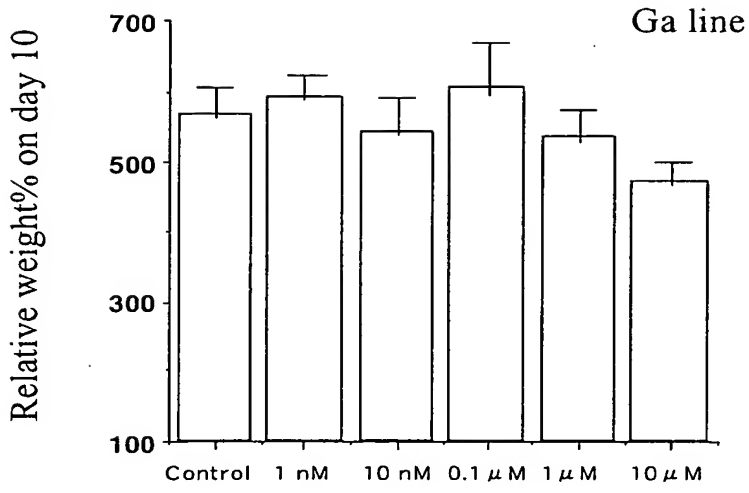
Ga line
Relative weight% on day 10
700
500
300
100
Control
1 nM
10 nM
0.1 μM
1 μM
10 μM
Chlorsulfuron concentration

Fig. 1 2

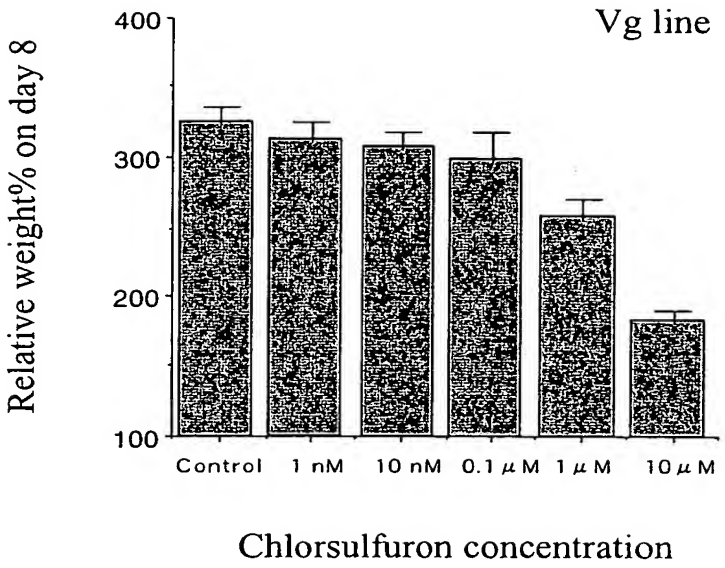
Vg line
Relative weight% on day 8
400
300
200
100
Control
1 nM
10 nM
0.1 μM
1 μM
10 μM
Chlorsulfuron concentration

Fig. 1 3

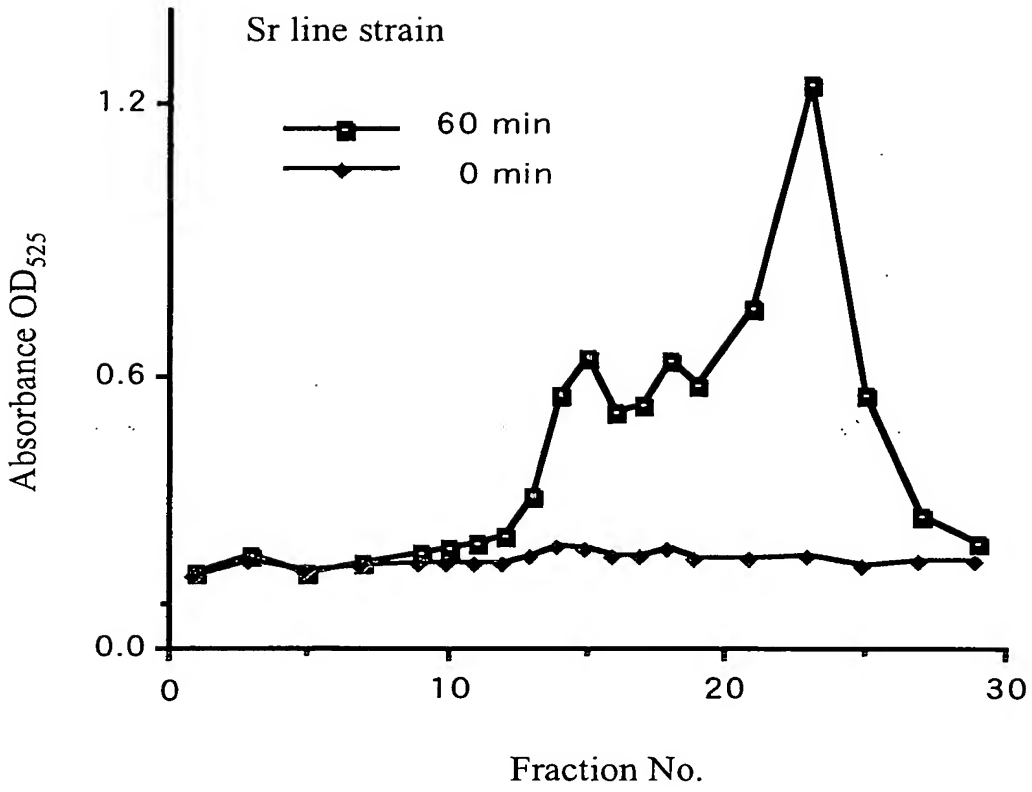
Sr line strain
60 min
0 min
1.2
0.6
0.0
Absorbance OD_{525}
0
10
20
30
Fraction No.

Fig. 1 4

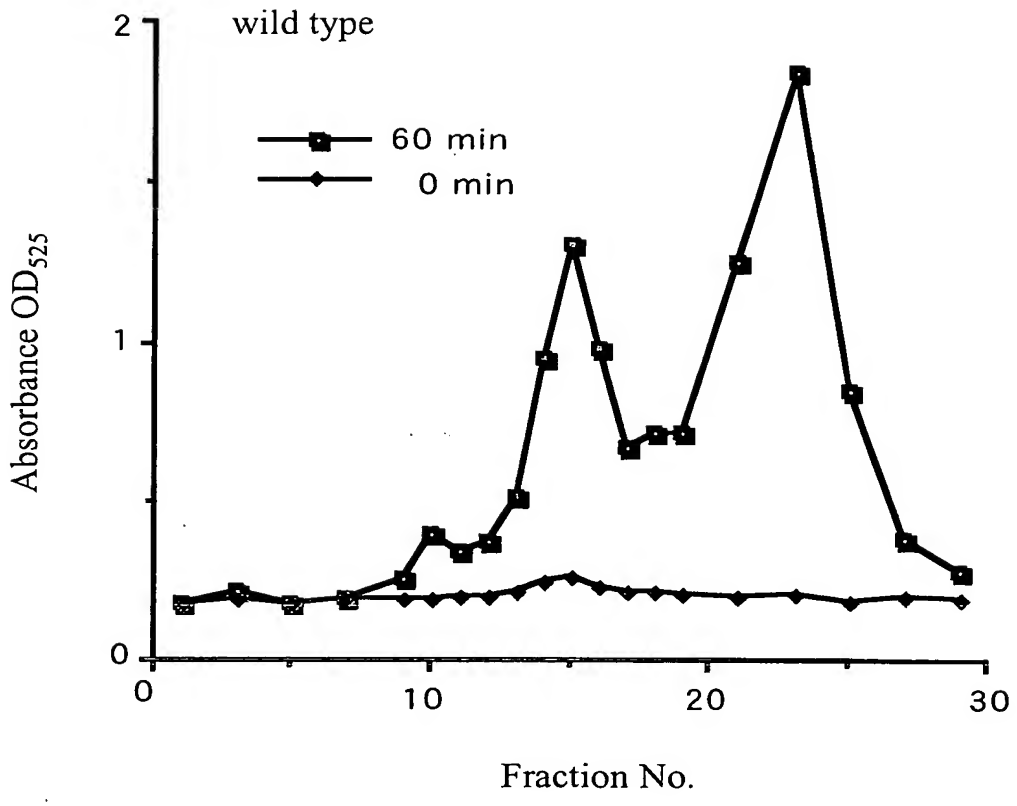
wild type
60 min
0 min
Absorbance OD_{525}
2
1
0
0
10
20
30
Fraction No.

Fig. 1 5

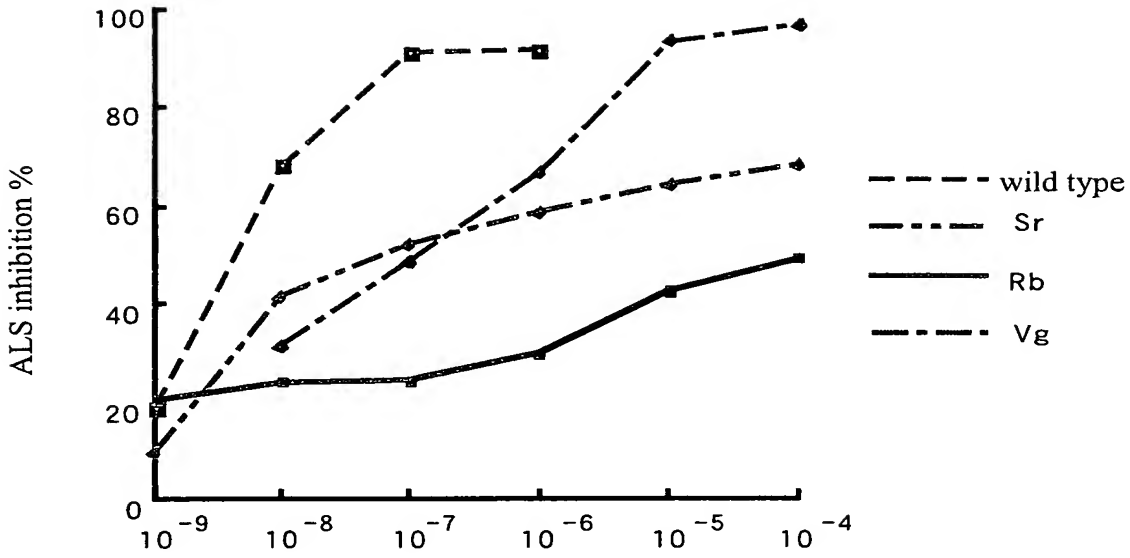
100
80
60
40
20
0
ALS inhibition %
10 -9
10 -8
10 -7
10 -6
10 -5
10 -4
wild type
Sr
Rb
Vg
Bispyribac-sodium concentration(M)

Fig. 1 6

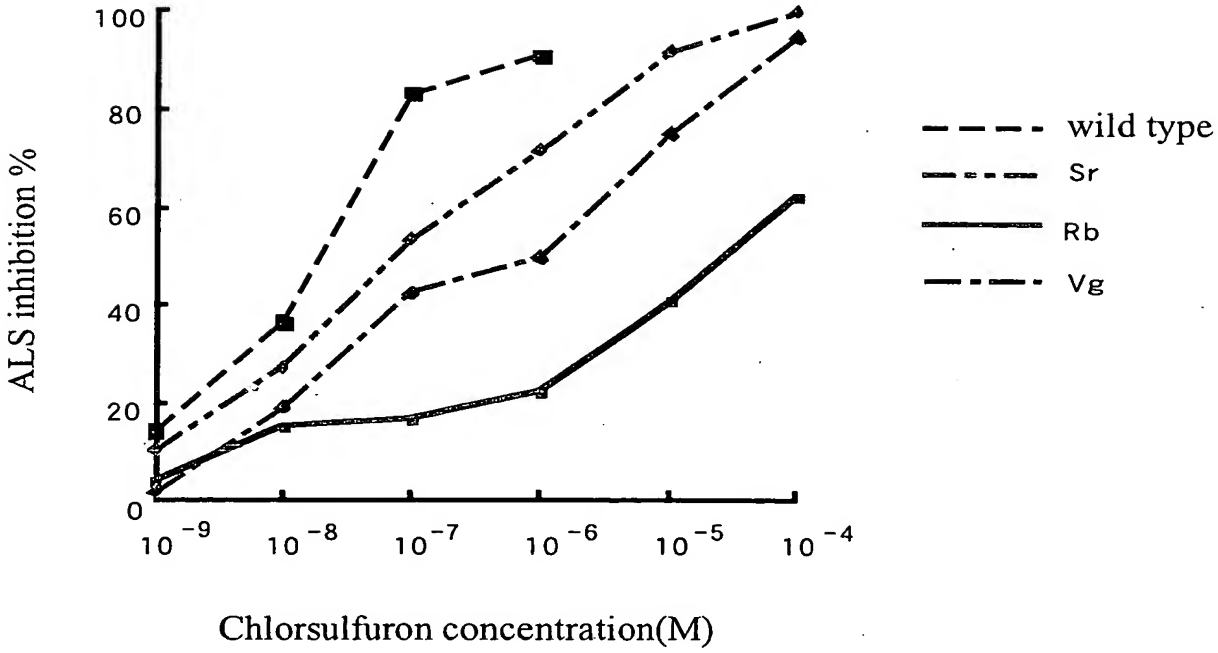
100
80
60
40
20
0
ALS inhibition %
10 -9
10 -8
10 -7
10 -6
10 -5
10 -4
Chlorsulfuron concentration(M)
wild type
Sr
Rb
Vg

Fig. 1 7

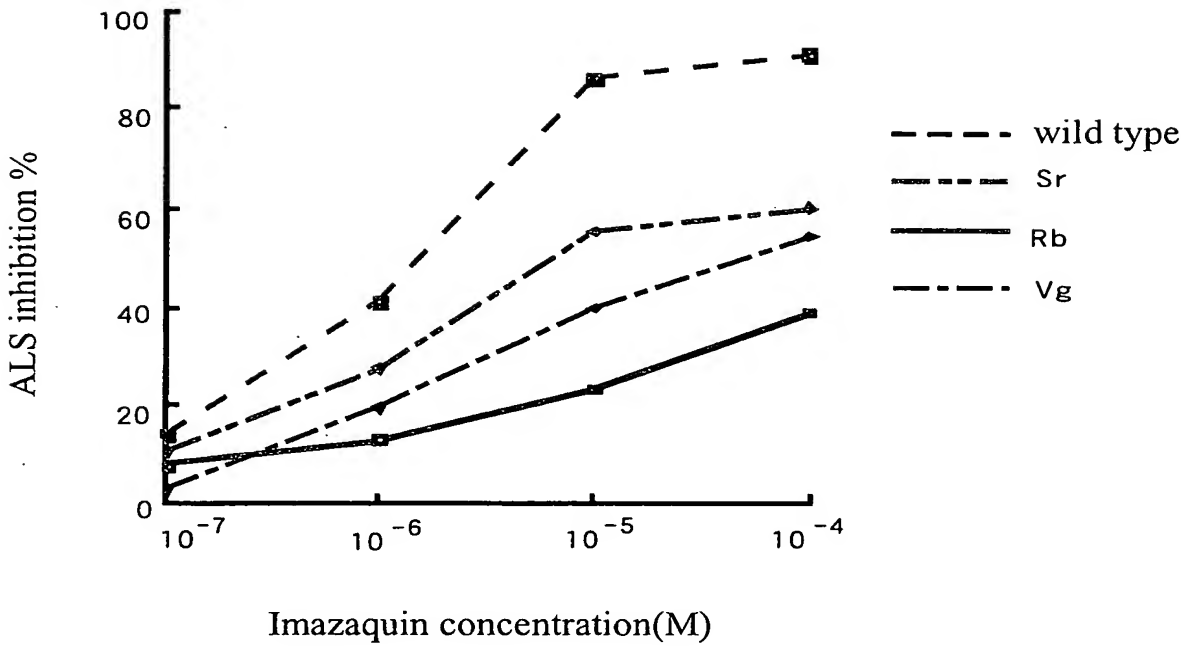
100
80
60
40
20
0
ALS inhibition %
10 -7
10 -6
10 -5
10 -4
Imazaquin concentration(M)
wild type
Sr
Rb
Vg

Fig. 18A

1st Nucleotide Sequence
File Name : Nipponbare ALS partial cDNA
Sequence Size : 1505

2nd Nucleotide Sequence
File Name : X63554 maize ALS 1
Sequence Size : 2544

```
    1'                                                    ACCCACGCGTCCGATGTGGAGGA
                                                          *** ** ** **
 1141" CATCGTCGAGGTCACCCGCTCCATCACCAAGCACAACTACCTGGTCCTCGACGTCGACGA

   24' CATCCCCCGCGTCATACAGGAAGCCTTCTTCCTCGCGTCCTCGGGCCGTCCTGGCCCGGT
        ************** * ***** ************** ***** ** ** ** ** *****
 1201" CATCCCCCGCGTCGTGCAGGAGGCCTTCTTCCTCGCATCCTCTGGTCGCCCGGGGCCGGT

   84' GCTGGTCGACATCCCCAAGGACATCCAGCAGCAGATGGCCGTGCCGGTCTGGGACACCTC
        *** ** ********************************** ******* *********  *
 1261" GCTTGTTGACATCCCCAAGGACATCCAGCAGCAGATGGCGGTGCCGGCCTGGGACACGCC

  144' GATGAATCTACCAGGGTACATCGCACGCCTGCCCAAGCCACCCGCGACAGAATTGCTTGA
        **** *** ** ********** ***** ******** ******** ***** *****
 1321" CATGAGTCTGCCTGGGTACATCGCGCGCCTTCCCAAGCCTCCCGCGACTGAATTTCTTGA

  204' GCAGGTCTTGCGTCTGGTTGGCGAGTCACGGCGCCCGATTCTCTATGTCGGTGGTGGCTG
        ******  ******* ***** ** **********  **** ***** ** ********
 1381" GCAGGTGCTGCGTCTTGTTGGTGAATCACGGCGCCCTGTTCTTTATGTTGGCGGTGGCTG

  264' CTCTGCATCTGGTGACGAATTGCGCTGGTTTGTTGAGCTGACTGGTATCCCAGTTACAAC
        * ***** ***** ** *** ** * ***** *** ******* ******** *****
 1441" TGCAGCATCAGGTGAGGAGTTGTGCCGCTTTGTGGAGTTGACTGGAATCCCAGTCACAAC

  324' CACTCTGATGGGCCTCGGCAATTTCCCCAGTGACGACCCGTTGTCCCTGCGCATGCTTGG
        ***** ******** ***** ******** ********  **** **************
 1501" TACTCTTATGGGCCTTGGCAACTTCCCCAGCGACGACCCACTGTCACTGCGCATGCTTGG

  384' GATGCATGGCACGGTGTACGCAAATTATGCCGTGGATAAGGCTGACCTGTTGCTTGCGTT
        *********** ***** *********** *********** ** *********** **
 1561" TATGCATGGCACAGTGTATGCAAATTATGCAGTGGATAAGGCCGATCTGTTGCTTGCATT

  444' TGGTGTGCGGTTTGATGATCGTGTGACAGGGAAAATTGAGGCTTTTGCAAGCAGGGCCAA
        ************************************************* **** ** **
 1621" TGGTGTGCGGTTTGATGATCGTGTGACAGGGAAAATTGAGGCTTTTGCAGGCAGAGCTAA

  504' GATTGTGCACATTGACATTGATCCAGCAGAGATTGGAAAGAACAAGCAACCACATGTGTC
        *************** ******** ** ******** *********** ***********
 1681" GATTGTGCACATTGATATTGATCCTGCTGAGATTGGCAAGAACAAGCAGCCACATGTGTC

  564' AATTTGCGCAGATGTTAAGCTTGCTTTACAGGGCTTGAATGCTCTGCTACAACAGAGCAC
        ** ** ******************** ****** ***** **** **  **   *****
 1741" CATCTGTGCAGATGTTAAGCTTGCTTTGCAGGGCATGAATACTCTTCTGGAAGGAAGCAC

  624' AACAAAGACAAGTTCTGATTTTAGTGCATGGCACAATGAGTTGGACCAGCAGAAGAGGGA
        * ******  ** * *** **  *  ********  **** ***** ***** *********
 1801" ATCAAAGAAGAGCTTTGACTTCGGCTCATGGCATGATGAATTGGATCAGCAAAAGAGGGA

  684' GTTTCCTCTGGGGTACAAAACTTTTGGTGAAGAGATCCCACCGCAATATGCCATTCAGGT
        ****** ** ** ** ****  **    *** ** ****  ** ******** *********
 1861" GTTTCCCCTTGGATATAAAATCTTCAATGAGGAAATCCAGCCACAATATGCTATTCAGGT

  744' GCTGGATGAGCTGACGAAAGGTGAGGCAATCATCGCTACTGGTGTTGGGCAGCACCAGAT
        ** ****** ******* ** ***** ***** ** ** ********************
 1921" TCTTGATGAGTTGACGAAGGGGGAGGCCATCATTGCCACAGGTGTTGGGCAGCACCAGAT

  804' GTGGGCGGCACAATATTACACCTACAAGCGGCCACGGCAGTGGCTGTCTTCGGCTGGTCT
        ************* ******** ************* ***************** *********
 1981" GTGGGCGGCACAGTATTACACTTACAAGCGGCCAAGGCAGTGGCTGTCTTCAGCTGGTCT

  864' GGGCGCAATGGGATTTGGGCTGCCTGCTGCAGCTGGTGCTTCTGTGGCTAACCCAGGTGT
        ** ** ************ **** ***** ********* ******* ***********
 2041" TGGGGCTATGGGATTTGGTTTGCCGGCTGCTGCTGGTGCTGCTGTGGCCAACCCAGGTGT

  924' CACAGTTGTTGATATTGATGGGGATGGTAGCTTCCTCATGAACATTCAGGAGCTGGCATT
        *** ******** ** ** ** ********************************** **  *
```

Fig. 18B

```
2101″ CACTGTTGTTGACATCGACGGAGATGGTAGCTTCCTCATGAACATTCAGGAGCTAGCTAT

 984' GATCCGCATTGAGAACCTCCCTGTGAAGGTGATGGTGTTGAACAACCAACATTTGGGTAT
      ****** ************** ** *****  * *** * ******** **  * ** **
2161″ GATCCGTATTGAGAACCTCCCAGTCAAGGTCTTTGTGCTAAACAACCAGCACCTCGGGAT

1044' GGTGGTGCAATGGGAGGATAGGTTTTACAAGGCGAATAGGGCGCATACATACTTGGGCAA
      ********* ******** ***** ** ***** ***** ** ** **** ****** **
2221″ GGTGGTGCAGTGGGAGGACAGGTTCTATAAGGCCAATAGAGCACACACATTCTTGGGAAA

1104' CCCGGAATGTGAGAGCGAGATATATCCAGATTTTGTGACCTATTGCTAAGGGGTTCAATA
      *** **    ** ** **********************  * ******** ******** *
2281″ CCCAGAGAACGAAAGTGAGATATATCCAGATTTTGTG-GCAATTGCTAAAGGGTTCAACA

1164' TTCCTGCAGTCCGTGTAACAAAGAAGAGTGAAGTCCGTGCCGCCATCAAGAAGATGCTCG
      **** *********** *********** ******* *** ** ************** *
2340″ TTCCAGCAGTCCGTGTGACAAAGAAGAGCGAAGTCCATGCAGCAATCAAGAAGATGCTTG

1224' AGACTCCAGGGCCATACTTGTTGGATATCATCGTCCCGCACCAGGAGCATGTGCTGCCTA
      ** ********** *** * ******** ************************ ******
2400″ AGGCTCCAGGGCCGTACCTCTTGGATATAATCGTCCCGCACCAGGAGCATGTGTTGCCTA

1284' TGATCCCAAGTGGGGGCGCATTCAAGGACATGATCCTGGATGGTGATGGCAGGACTGTGT
      ******* ***** ** ** ******** ******************************
2460″ TGATCCCTAGTGGTGGGGCTTTCAAGGATATGATCCTGGATGGTGATGGCAGGACTGTGT

1344' ATTAATCTATAATCTGTATGTTGGCAAAGCACCAGCCCGGCCTATGTTTGACCTGAATGA
      *** ***  *   *** * ** * *
2520″ ATTGATCCGTTGACTGCAGGTCGAC
```

Fig. 19A

1st Nucleotide Sequence
File Name : 2-point mutant full-length ALS cDNA
2nd Nucleotide Sequence
File Name : wild type full-length ALS cDNA

```
    1'                  CTCGCCGCCGCCGCCGCCGCCACCACCCACCATGGCTACGACCG
                        ********************************************
   1" CCCAAACCCAGAAACCCTCGCCGCCGCCGCCGCCGCCACCACCCACCATGGCTACGACCG

   45' CCGCGGCCGCGGCCGCCGCCCTGTCCGCCGCCGCGACGGCCAAGACCGGCCGTAAGAACC
       ************************************************************
   61" CCGCGGCCGCGGCCGCCGCCCTGTCCGCCGCCGCGACGGCCAAGACCGGCCGTAAGAACC

  105' ACCAGCGACACCACGTCCTTCCCGCTCGAGGCCGGGTGGGGGCGGCGGCGGTCAGGTGCT
       ************************************************************
  121" ACCAGCGACACCACGTCCTTCCCGCTCGAGGCCGGGTGGGGGCGGCGGCGGTCAGGTGCT

  165' CGGCGGTGTCCCCGGTCACCCCGCCGTCCCCGGCGCCGCCGGCCACGCCGCTCCGGCCGT
       ************************************************************
  181" CGGCGGTGTCCCCGGTCACCCCGCCGTCCCCGGCGCCGCCGGCCACGCCGCTCCGGCCGT

  225' GGGGGCCGGCCGAGCCCCGCAAGGGCGCGGACATCCTCGTGGAGGCGCTGGAGCGGTGCG
       ************************************************************
  241" GGGGGCCGGCCGAGCCCCGCAAGGGCGCGGACATCCTCGTGGAGGCGCTGGAGCGGTGCG

  285' GCGTCAGCGACGTGTTCGCCTACCCGGGCGGCGCGTCCATGGAGATCCACCAGGCGCTGA
       ************************************************************
  301" GCGTCAGCGACGTGTTCGCCTACCCGGGCGGCGCGTCCATGGAGATCCACCAGGCGCTGA

  345' CGCGCTCCCCGGTCATCACCAACCACCTCTTCCGCCACGAGCAGGGCGAGGCGTTCGCGG
       ************************************************************
  361" CGCGCTCCCCGGTCATCACCAACCACCTCTTCCGCCACGAGCAGGGCGAGGCGTTCGCGG

  405' CGTCCGGGTACGCGCGCGCGTCCGGCCGCGTCGGGGTCTGCGTCGCCACCTCCGGCCCCG
       ************************************************************
  421" CGTCCGGGTACGCGCGCGCGTCCGGCCGCGTCGGGGTCTGCGTCGCCACCTCCGGCCCCG

  465' GGGCAACCAACCTCGTGTCCGCGCTCGCCGACGCGCTGCTCGACTCCGTCCCGATGGTCG
       ************************************************************
  481" GGGCAACCAACCTCGTGTCCGCGCTCGCCGACGCGCTGCTCGACTCCGTCCCGATGGTCG

  525' CCATCACGGGCCAGGTCCCCCGCCGCATGATCGGCACCGACGCCTTCCAGGAGACGCCCA
       ************************************************************
  541" CCATCACGGGCCAGGTCCCCCGCCGCATGATCGGCACCGACGCCTTCCAGGAGACGCCCA

  585' TAGTCGAGGTCACCCGCTCCATCACCAAGCACAATTACCTTGTCCTTGATGTGGAGGACA
       ************************************************************
  601" TAGTCGAGGTCACCCGCTCCATCACCAAGCACAATTACCTTGTCCTTGATGTGGAGGACA

  645' TCCCCCGCGTCATACAGGAAGCCTTCTTCCTCGCGTCCTCGGGCCGTCCTGGCCCGGTGC
       ************************************************************
  661" TCCCCCGCGTCATACAGGAAGCCTTCTTCCTCGCGTCCTCGGGCCGTCCTGGCCCGGTGC

  705' TGGTCGACATCCCCAAGGACATCCAGCAGCAGATGGCCGTGCCGGTCTGGGACACCTCGA
       ************************************************************
  721" TGGTCGACATCCCCAAGGACATCCAGCAGCAGATGGCCGTGCCGGTCTGGGACACCTCGA

  765' TGAATCTACCAGGGTACATCGCACGCCTGCCCAAGCCACCCGCGACAGAATTGCTTGAGC
       ************************************************************
  781" TGAATCTACCAGGGTACATCGCACGCCTGCCCAAGCCACCCGCGACAGAATTGCTTGAGC

  825' AGGTCTTGCGTCTGGTTGGCGAGTCACGGCGCCCGATTCTCTATGTCGGTGGTGGCTGCT
       ************************************************************
  841" AGGTCTTGCGTCTGGTTGGCGAGTCACGGCGCCCGATTCTCTATGTCGGTGGTGGCTGCT

  885' CTGCATCTGGTGACGAATTGCGCTGGTTTGTTGAGCTGACTGGTATCCCAGTTACAACCA
       ************************************************************
  901" CTGCATCTGGTGACGAATTGCGCTGGTTTGTTGAGCTGACTGGTATCCCAGTTACAACCA

  945' CTCTGATGGGCCTCGGCAATTTCCCCAGTGACGACCCGTTGTCCCTGCGCATGCTTGGGA
       ************************************************************
  961" CTCTGATGGGCCTCGGCAATTTCCCCAGTGACGACCCGTTGTCCCTGCGCATGCTTGGGA

 1005' TGCATGGCACGGTGTACGCAAATTATGCCGTGGATAAGGCTGACCTGTTGCTTGCGTTTG
```

Fig. 19B

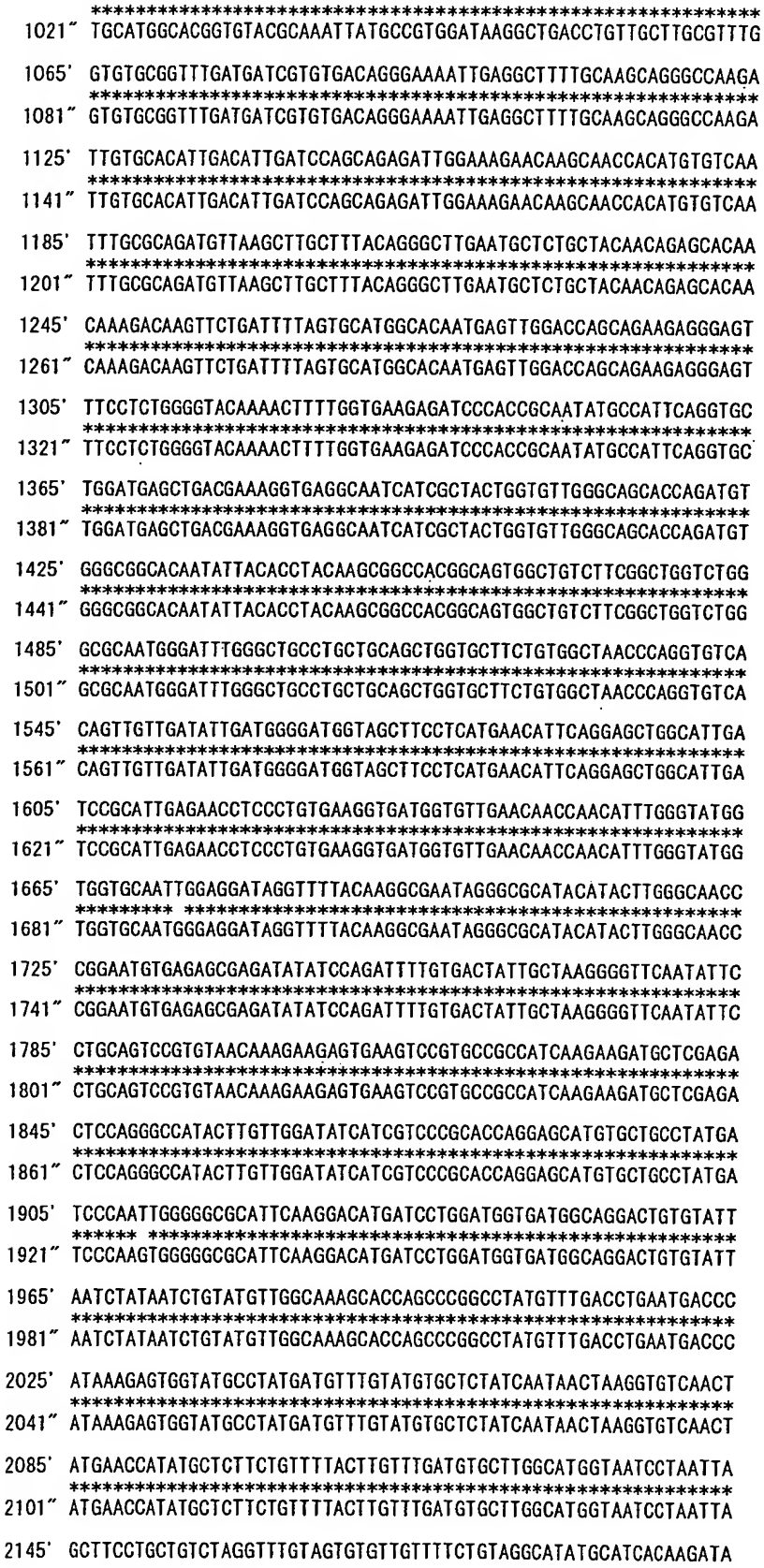
1021″ TGCATGGCACGGTGTACGCAAATTATGCCGTGGATAAGGCTGACCTGTTGCTTGCGTTTG
1065' GTGTGCGGTTTGATGATCGTGTGACAGGGAAAATTGAGGCTTTTGCAAGCAGGGCCAAGA
1081″ GTGTGCGGTTTGATGATCGTGTGACAGGGAAAATTGAGGCTTTTGCAAGCAGGGCCAAGA
1125' TTGTGCACATTGACATTGATCCAGCAGAGATTGGAAAGAACAAGCAACCACATGTGTCAA
1141″ TTGTGCACATTGACATTGATCCAGCAGAGATTGGAAAGAACAAGCAACCACATGTGTCAA
1185' TTTGCGCAGATGTTAAGCTTGCTTTACAGGGCTTGAATGCTCTGCTACAACAGAGCACAA
1201″ TTTGCGCAGATGTTAAGCTTGCTTTACAGGGCTTGAATGCTCTGCTACAACAGAGCACAA
1245' CAAAGACAAGTTCTGATTTTAGTGCATGGCACAATGAGTTGGACCAGCAGAAGAGGGAGT
1261″ CAAAGACAAGTTCTGATTTTAGTGCATGGCACAATGAGTTGGACCAGCAGAAGAGGGAGT
1305' TTCCTCTGGGGTACAAAACTTTTGGTGAAGAGATCCCACCGCAATATGCCATTCAGGTGC
1321″ TTCCTCTGGGGTACAAAACTTTTGGTGAAGAGATCCCACCGCAATATGCCATTCAGGTGC
1365' TGGATGAGCTGACGAAAGGTGAGGCAATCATCGCTACTGGTGTTGGGCAGCACCAGATGT
1381″ TGGATGAGCTGACGAAAGGTGAGGCAATCATCGCTACTGGTGTTGGGCAGCACCAGATGT
1425' GGGCGGCACAATATTACACCTACAAGCGGCCACGGCAGTGGCTGTCTTCGGCTGGTCTGG
1441″ GGGCGGCACAATATTACACCTACAAGCGGCCACGGCAGTGGCTGTCTTCGGCTGGTCTGG
1485' GCGCAATGGGATTTGGGCTGCCTGCTGCAGCTGGTGCTTCTGTGGCTAACCCAGGTGTCA
1501″ GCGCAATGGGATTTGGGCTGCCTGCTGCAGCTGGTGCTTCTGTGGCTAACCCAGGTGTCA
1545' CAGTTGTTGATATTGATGGGGATGGTAGCTTCCTCATGAACATTCAGGAGCTGGCATTGA
1561″ CAGTTGTTGATATTGATGGGGATGGTAGCTTCCTCATGAACATTCAGGAGCTGGCATTGA
1605' TCCGCATTGAGAACCTCCCTGTGAAGGTGATGGTGTTGAACAACCAACATTTGGGTATGG
1621″ TCCGCATTGAGAACCTCCCTGTGAAGGTGATGGTGTTGAACAACCAACATTTGGGTATGG
1665' TGGTGCAATTGGAGGATAGGTTTTACAAGGCGAATAGGGCGCATACATACTTGGGCAACC
1681″ TGGTGCAATGGGAGGATAGGTTTTACAAGGCGAATAGGGCGCATACATACTTGGGCAACC
1725' CGGAATGTGAGAGCGAGATATATCCAGATTTTGTGACTATTGCTAAGGGGTTCAATATTC
1741″ CGGAATGTGAGAGCGAGATATATCCAGATTTTGTGACTATTGCTAAGGGGTTCAATATTC
1785' CTGCAGTCCGTGTAACAAAGAAGAGTGAAGTCCGTGCCGCCATCAAGAAGATGCTCGAGA
1801″ CTGCAGTCCGTGTAACAAAGAAGAGTGAAGTCCGTGCCGCCATCAAGAAGATGCTCGAGA
1845' CTCCAGGGCCATACTTGTTGGATATCATCGTCCCGCACCAGGAGCATGTGCTGCCTATGA
1861″ CTCCAGGGCCATACTTGTTGGATATCATCGTCCCGCACCAGGAGCATGTGCTGCCTATGA
1905' TCCCAATTGGGGGCGCATTCAAGGACATGATCCTGGATGGTGATGGCAGGACTGTGTATT
1921″ TCCCAAGTGGGGGCGCATTCAAGGACATGATCCTGGATGGTGATGGCAGGACTGTGTATT
1965' AATCTATAATCTGTATGTTGGCAAAGCACCAGCCCGGCCTATGTTTGACCTGAATGACCC
1981″ AATCTATAATCTGTATGTTGGCAAAGCACCAGCCCGGCCTATGTTTGACCTGAATGACCC
2025' ATAAAGAGTGGTATGCCTATGATGTTTGTATGTGCTCTATCAATAACTAAGGTGTCAACT
2041″ ATAAAGAGTGGTATGCCTATGATGTTTGTATGTGCTCTATCAATAACTAAGGTGTCAACT
2085' ATGAACCATATGCTCTTCTGTTTTACTTGTTTGATGTGCTTGGCATGGTAATCCTAATTA
2101″ ATGAACCATATGCTCTTCTGTTTTACTTGTTTGATGTGCTTGGCATGGTAATCCTAATTA
2145' GCTTCCTGCTGTCTAGGTTTGTAGTGTGTTGTTTTCTGTAGGCATATGCATCACAAGATA

Fig. 19C

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          ************************************************************
2161″ GCTTCCTGCTGTCTAGGTTTGTAGTGTGTTGTTTTCTGTAGGCATATGCATCACAAGATA

2205' TCATGTAAGTTTCTTGTCCTACATATCAATAATAAGAGAATAAAGTACTTCTATGTAAAA
          ************************************************** ****
2221″ TCATGTAAGTTTCTTGTCCTACATATCAATAATAAGAGAATAAAGTACTTCTATGCAAAA

2265' AAAAAAAAAAAAAA
          **************
2281″ AAAAAAAAAAAAAAAAAAAA
```

Fig. 2 0

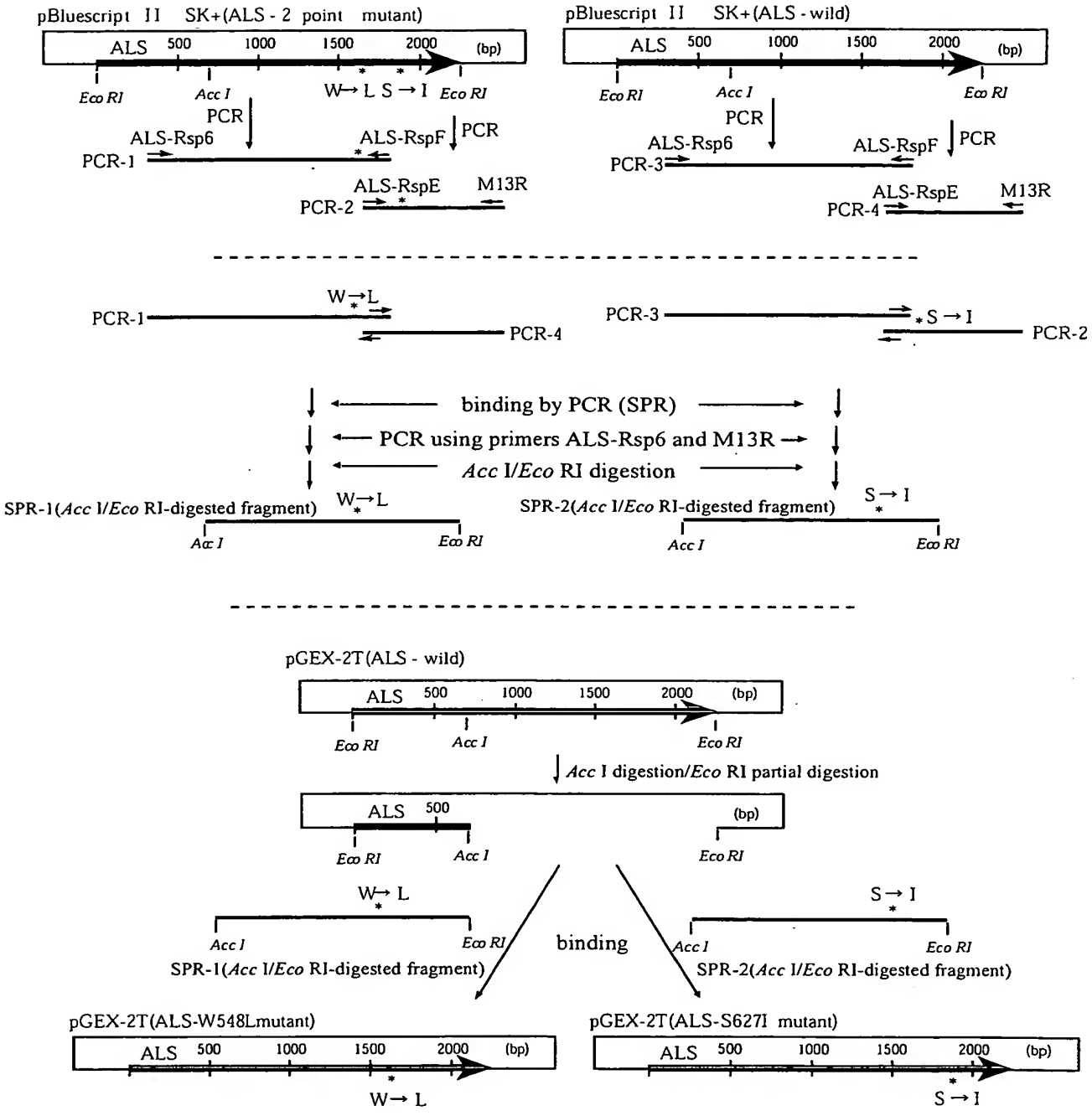

pBluescript II SK+(ALS - 2 point mutant)
ALS 500 1000 1500 2000 (bp)
Eco RI
Acc I
W→ L S → I
Eco RI
PCR
ALS-Rsp6
ALS-RspF
PCR
PCR-1
ALS-RspE
M13R
PCR-2
pBluescript II SK+(ALS - wild)
ALS 500 1000 1500 2000 (bp)
Eco RI
Acc I
Eco RI
PCR
ALS-Rsp6
ALS-RspF
PCR
PCR-3
ALS-RspE
M13R
PCR-4
W→L
PCR-1
PCR-4
PCR-3
S → I
PCR-2
binding by PCR (SPR)
PCR using primers ALS-Rsp6 and M13R
Acc I/Eco RI digestion
SPR-1(Acc I/Eco RI-digested fragment)
W→L
Acc I
Eco RI
SPR-2(Acc I/Eco RI-digested fragment)
S → I
Acc I
Eco RI
pGEX-2T(ALS - wild)
ALS 500 1000 1500 2000 (bp)
Eco RI
Acc I
Eco RI
Acc I digestion/Eco RI partial digestion
ALS 500
(bp)
Eco RI
Acc I
Eco RI
W→ L
Acc I
Eco RI
SPR-1(Acc I/Eco RI-digested fragment)
binding
S → I
Acc I
Eco RI
SPR-2(Acc I/Eco RI-digested fragment)
pGEX-2T(ALS-W548Lmutant)
ALS 500 1000 1500 2000 (bp)
W→ L
pGEX-2T(ALS-S627I mutant)
ALS 500 1000 1500 2000 (bp)
S → I

Fig. 2 1

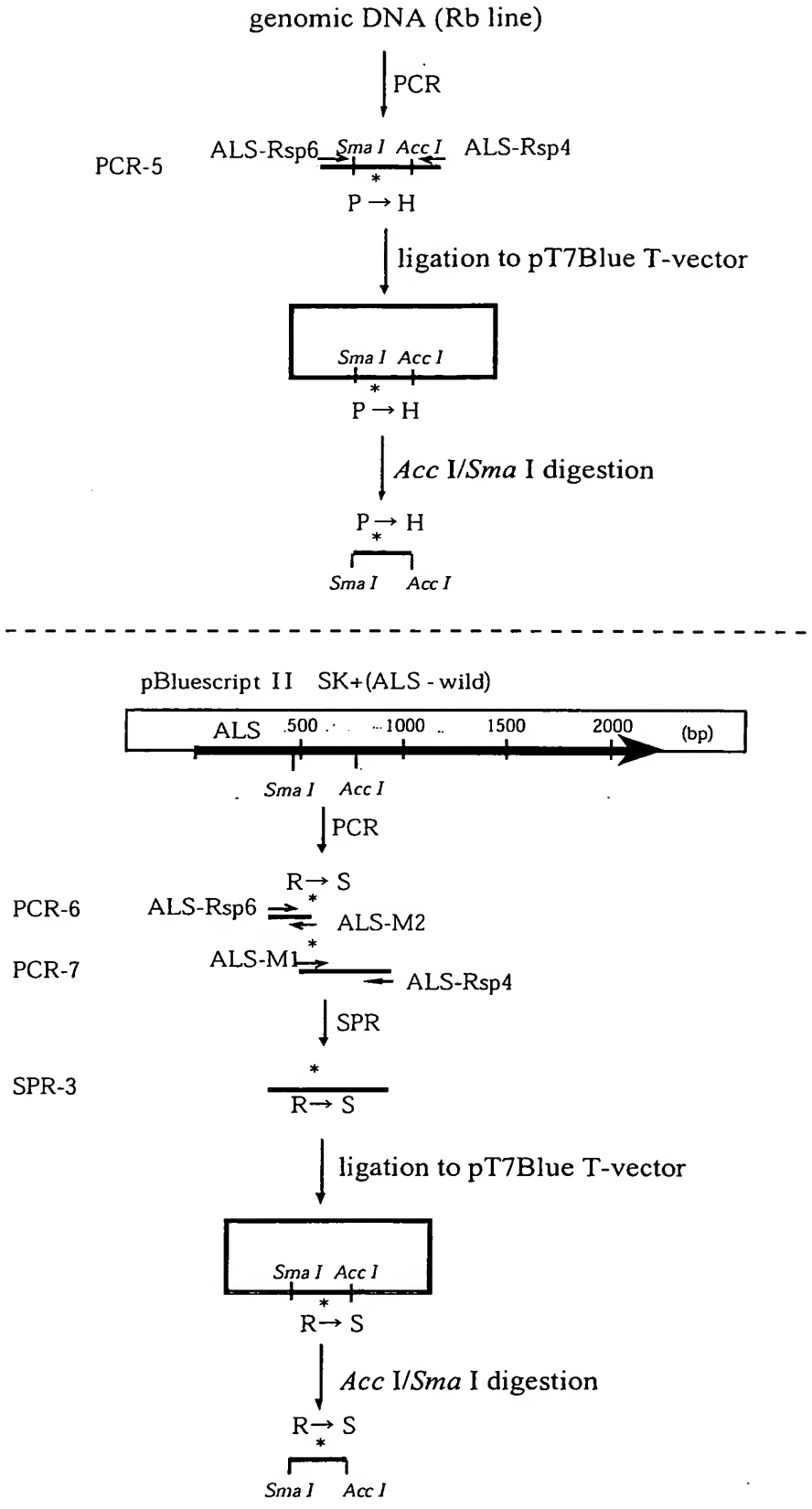

genomic DNA (Rb line)
PCR
PCR-5
ALS-Rsp6
Sma I
Acc I
ALS-Rsp4
P → H
ligation to pT7Blue T-vector
Sma I Acc I
P → H
Acc I/Sma I digestion
P → H
Sma I
Acc I
pBluescript II SK+(ALS - wild)
ALS
500
1000
1500
2000
(bp)
Sma I
Acc I
PCR
R → S
PCR-6
ALS-Rsp6
ALS-M2
PCR-7
ALS-M1
ALS-Rsp4
SPR
SPR-3
R → S
ligation to pT7Blue T-vector
Sma I Acc I
R → S
Acc I/Sma I digestion
R → S
Sma I
Acc I

Fig. 2 2

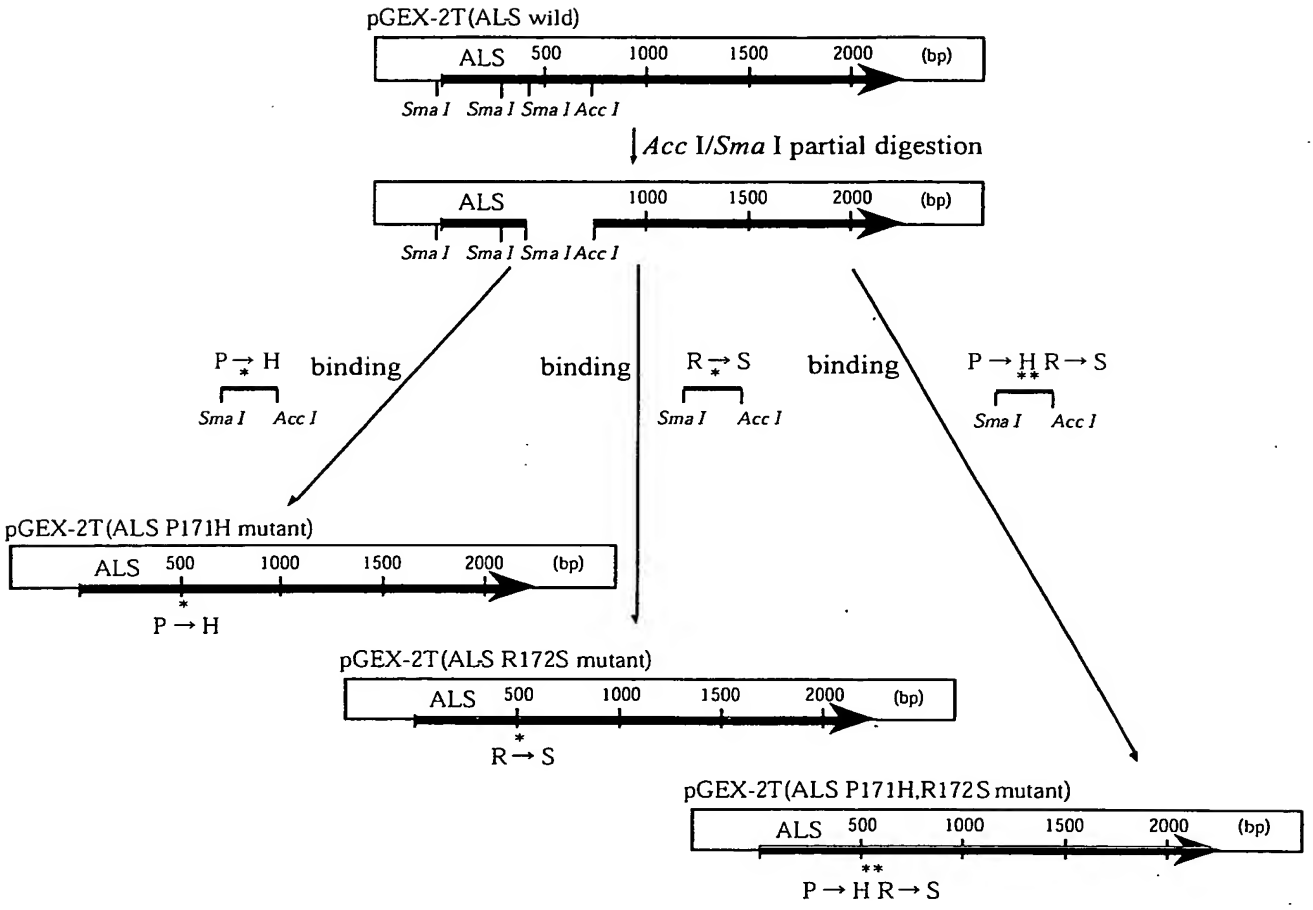

pGEX-2T(ALS wild)
ALS
500
1000
1500
2000
(bp)
Sma I
Sma I
Sma I
Acc I
Acc I/Sma I partial digestion
P → H
binding
R → S
binding
P → H R → S
binding
pGEX-2T(ALS P171H mutant)
P → H
pGEX-2T(ALS R172S mutant)
R → S
pGEX-2T(ALS P171H,R172S mutant)
P → H R → S

Fig. 2 3

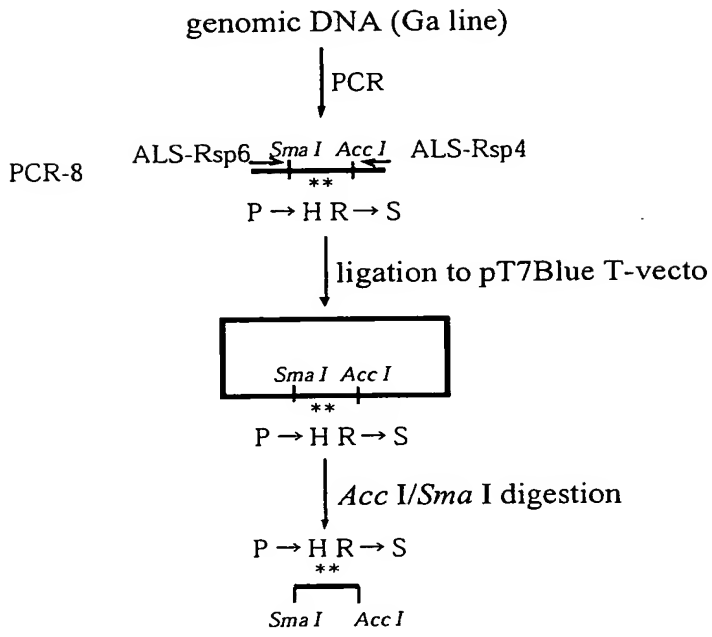

genomic DNA (Ga line)
PCR
PCR-8
ALS-Rsp6
Sma I
Acc I
ALS-Rsp4
**
P → H R → S
ligation to pT7Blue T-vecto
Sma I
Acc I
**
P → H R → S
Acc I/Sma I digestion
P → H R → S
**
Sma I
Acc I

Fig. 2 4

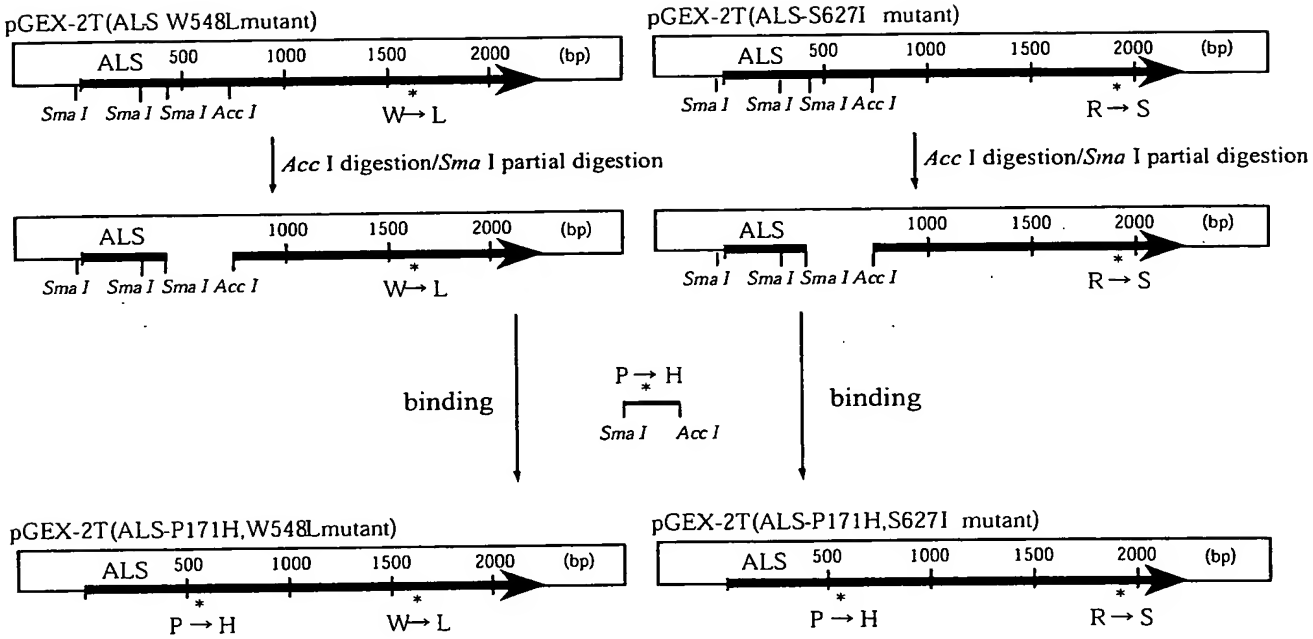

pGEX-2T(ALS W548Lmutant)
ALS
500
1000
1500
2000
(bp)
Sma I
Sma I
Sma I
Acc I
W→L
pGEX-2T(ALS-S627I mutant)
R→S
Acc I digestion/Sma I partial digestion
binding
P→H
pGEX-2T(ALS-P171H,W548Lmutant)
pGEX-2T(ALS-P171H,S627I mutant)

Fig. 2 5

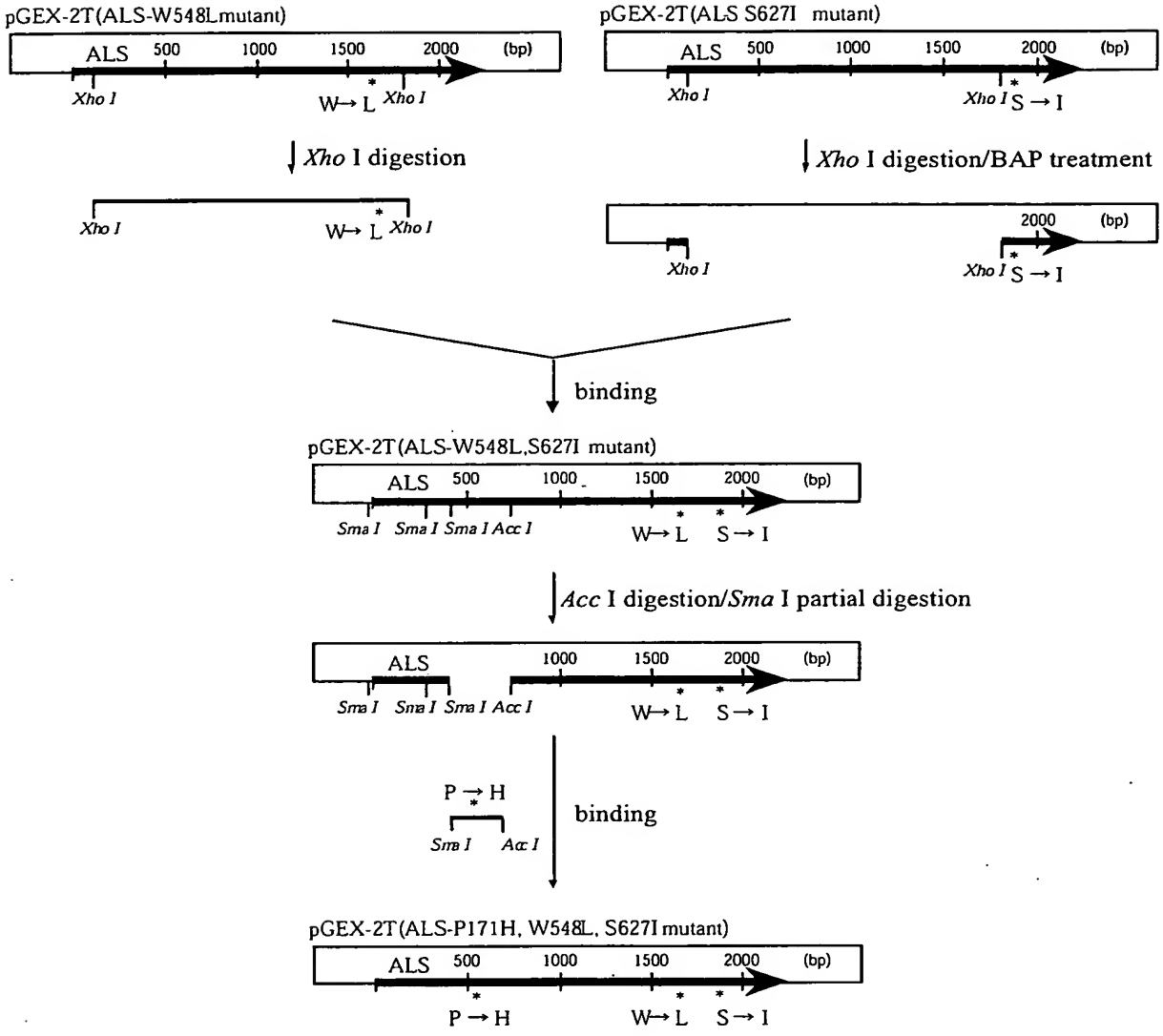

pGEX-2T(ALS-W548Lmutant)
ALS
500
1000
1500
2000
(bp)
Xho I
W→ L
Xho I
Xho I digestion
Xho I
W→ L
Xho I
pGEX-2T(ALS S627I mutant)
ALS
500
1000
1500
2000
(bp)
Xho I
Xho I
S → I
Xho I digestion/BAP treatment
2000
(bp)
Xho I
Xho I
S → I
binding
pGEX-2T(ALS-W548L,S627I mutant)
ALS
500
1000
1500
2000
(bp)
Sma I
Sma I
Sma I
Acc I
W→ L
S → I
Acc I digestion/Sma I partial digestion
ALS
1000
1500
2000
(bp)
Sma I
Sma I
Sma I
Acc I
W→ L
S → I
P → H
Sma I
Acc I
binding
pGEX-2T(ALS-P171H, W548L, S627I mutant)
ALS
500
1000
1500
2000
(bp)
P → H
W→ L
S → I

Fig. 2 6

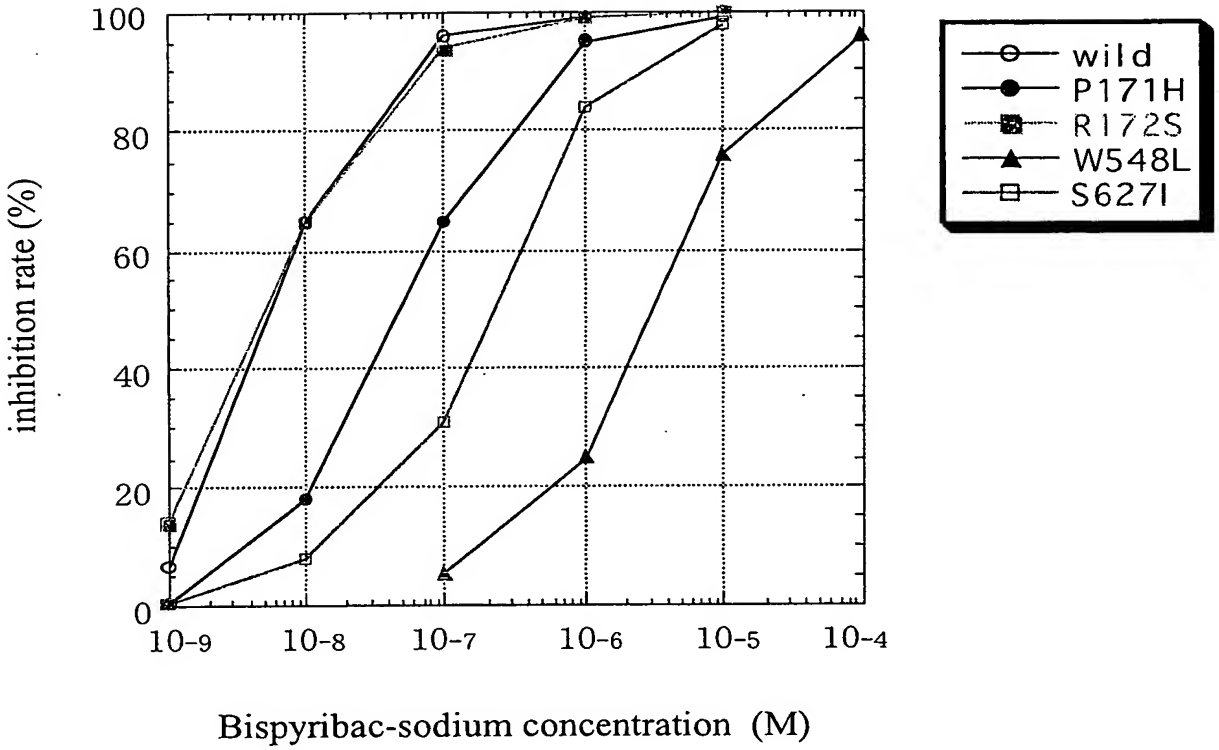
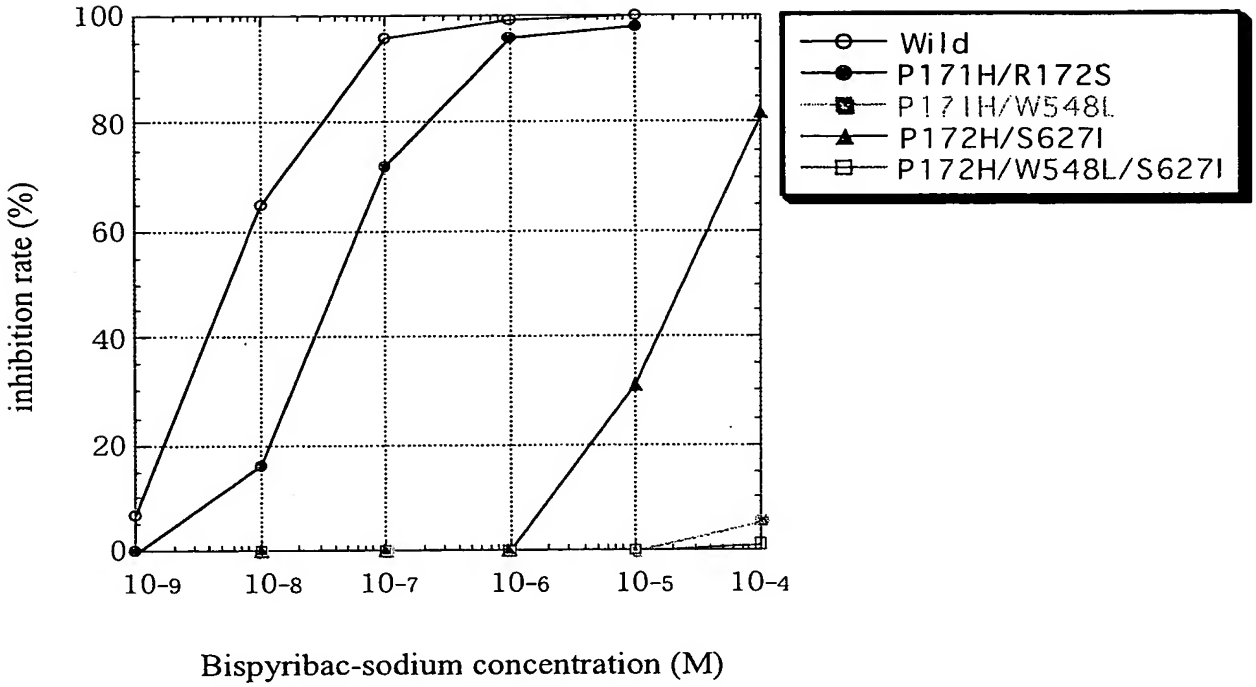

100
80
60
40
20
0
inhibition rate (%)
10-9
10-8
10-7
10-6
10-5
10-4
Bispyribac-sodium concentration (M)
wild
P171H
R172S
W548L
S627I

Fig. 2 7


100
80
60
40
20
0
inhibition rate (%)
10-9
10-8
10-7
10-6
10-5
10-4
Bispyribac-sodium concentration (M)
Wild
P171H/R172S
P171H/W548L
P172H/S627I
P172H/W548L/S627I